THE YEAR BOOK *of* DERMATOLOGY *and* SYPHILOLOGY

(1956-1957 YEAR BOOK *Series*)

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THE PRACTICAL MEDICINE YEAR BOOKS

This volume is one of the 14 comprising the Practical Medicine Series of Year Books founded in 1900 by C P Head, M.D and C. J Head, and published continuously since then. The complete list follows:

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INTRODUCTION

During the past year there has been further extensive and careful clinical appraisal in dermatology of therapy with drugs which have been introduced in recent years In view of the tendency to chronicity of certain of the dermatoses for which these medicaments are used interest has centered particularly on the effects of long term administration of the corticosteroids, antibiotics, antimalarials and other systemically given drugs.

Among the newer wide spectrum antibiotics novobiocin thus far has failed to show any particular virtues for systemic dermatologic use but appears to cause a prohibitively high incidence of drug eruptions On the other hand experience with tetracycline and related compounds generally has been favorable Drug eruptions, aside from monilial complications have been remarkably few indeed. Much has been said regarding the potential dangers of the prolonged use of oral antibiotics among them failure of the dermatosis under treatment to continue to respond favorably to the drug and development of resistant strains of micro-organisms which eventually might cause serious harm to the patient. The literature seems to support the experience of the editors who have not seen such effects even after many months to years of systemic therapy for acne furunculosis etc., with tetracycline and related compounds. When administered under careful medical supervision, these antibiotics have proved both safe and effective for long term as well as short term administration

The antimalarial drugs have also received extensive clinical trial In addition to their beneficial use in the management of lupus erythematosus and hypersensitivities to light, other possible dermatologic applications have been investigated and a search is being made for similarly effective compounds with better therapeutic ratios, i.e. greater efficacy and lower toxicity and sensitizing capacity Moreover the mechanisms underlying the anti-inflammatory action of these drugs have been the subject of several studies.

Among the recently introduced drugs great hope was held

ALLERGIC ECZEMATOUS CONTACT DERMATITIS

A Review of Selected Aspects For The Practitioner*

By Rudolf L. Baer and Victor H. Witten

PART I

Although isolated segments of the topic of allergic eczematous contact dermatitis have been dealt with in these Year Books from time to time over a period of years the editors here present a more general review of this highly important subject. It should be stressed at the outset, however that because of the wealth of information available in this area of dermatology even such a review of necessity must be highly selective and that it can cover only some of the newer findings together with certain of the older and well-established features.

Many terms have been used for the eczematous eruptions which result from external exposure of allergically hypersensitive skin to allergenic substances; the one which, in our opinion, is most descriptive is allergic eczematous contact dermatitis. Contact dermatitis, dermatitis venenata, eczematous dermatitis and allergic eczema are among the other frequently used synonyms. The name contact-*type* allergic eczematous dermatitis is also widely used. This term is broader and includes those eczematous eruptions of similar allergic etiology but resulting from exposures other than by way of external contact, e.g. ingestion, inhalation injection absorption through mucous membranes, etc. (to be discussed later).

CLINICAL MORPHOLOGY AND SYMPTOMATOLOGY

The clinical diagnosis of allergic eczematous contact dermatitis in its acute phase as a rule can be made without difficulty although its morphology may be quite atypical at

*From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman) and the Skin and Cancer Unit of the New York University Hospital.

The names of authors who have done original work referred to in this article and the references to their work have been omitted from the text. At the end of the article a list of some of the pertinent references is given.

out by some physicians that the ataractics or tranquilizers might prove helpful in the management of various dermatoses In general these preparations have done little good in skin diseases, except that they exert a calming influence on some patients Probably they have helped some patients to accept their skin diseases and live with them more happily! The tranquilizers perhaps have had the opposite of a calming effect on those physicians who have seen their patients develop drug eruptions and even nonthrombocytopenic purpuras due to these drugs

It is encouraging to see the increasing interest in x radiation of softer quality which as seems reasonable is particularly suitable for the treatment of those benign dermatoses which are superficial in nature Thus radiation in the grenz ray range (i e from 18 to 36 microns of aluminum half value layer) and also very soft x rays (i.e., less than 0.5 mm of aluminum half value layer) are finding increasing popularity The growing concern about the possible long term genetic effects of the more penetrating forms of radiation therapy may be expected to accelerate this trend

Much work has been done on hypo- and agammaglobulin

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basic sciences is increasingly employing the modern methods and tools of investigation including radioactive isotopes histochemical technics and immunologic methods varying from extremely refined serologic procedures to transfers of white

s this year is

human skin

with Treponema pallidum and of nails with pathogenic fungi The authors of these studies as well as the human subjects who volunteered have made a real contribution to important problems in syphilology and dermatologic mycology

—The Editors

IMMUNOLOGIC CONSIDERATIONS

From the practical point of view there is hardly any substance, whether it be animal, vegetable or mineral, which on occasion cannot be or has not been the cause of allergic eczematous contact dermatitis. As will be pointed out later on however the capacity of various substances to engender allergic eczematous sensitization differs tremendously. The more highly allergenic a substance the more likely it is to produce sensitization in susceptible persons on first exposure following one of the early contacts with the skin; the lower the sensitizing capacity of a substance, the less likely it is to produce sensitization on first exposure even in susceptible persons. Here repeated exposures are usually required. While these statements generally hold true, they cannot, of course, be accepted as an absolute rule.

The period during which sensitization fails to develop despite one or more adequate exposures to an allergen has been named the *period of refractoriness to sensitization*. This period may be virtually nonexistent, in which event the development of sensitization begins immediately on first exposure to the allergen; on the other hand it may vary from a few minutes or hours to many years. And, of course, most individuals fortunately never develop allergic sensitization to the vast majority of materials with which they come in contact despite a lifetime of exposures.

Once the mechanism of allergic sensitization has been set into motion, it takes anywhere from 5 days to several weeks, usually no more than 21 days, for the sensitivity to develop to a degree where, in the presence of the allergenic substance, clinically evident allergic reaction occurs. This very conspicuous interval corresponds to the incubation period as seen in the infection exanthemas, in the infectious diseases due to fungi, bacteria, etc., and in classic serum disease as first interpreted by von Pirquet and Schick. Therefore, the time which elapses between the actual sensitizing exposure to the allergen and the development of allergic sensitivity of sufficient degree to lead to clinical signs and symptoms on exposure to the allergen has been called the *period of incubation of sensitivity*. It should be noted that within the time period of 5 days to about 3 weeks the length of the incubation

times or may be mistaken for some similar eczematous eruption Most typical is the dermatitis which at the onset presents an area of erythema and later becomes slightly edematous and undergoes definite papulation and vesiculation Small areas may gradually increase in size and new ones appear either in the vicinity of the original lesions or at distant and apparently unrelated sites It is not unusual for adjacent plaques to become confluent thus forming larger areas of involvement

While the eruption as just described is the most typical and classic variety of allergic eczematous contact dermatitis one must be aware of the fact that the resulting dermatitis may vary in degree depending on the *intensity of the allergenic exposure the degree of existing allergic sensitivity the duration and frequency of exposure and the particular skin area affected* Thus the involvement may vary in size from a few millimeters to that of essentially the entire body and in addition the intensity can range from the slightest barely noticeable erythema to a hyperacute edematous and vesiculobullous eruption with oozing weeping and crusting or to a chronic torpid thickened hyperpigmented ill-defined eruption with hardly any signs of inflammation and complete absence of clinical papulation or vesiculation These extreme differences in the appearance of allergic eczematous contact dermatitis are important not only with regard to establishing the diagnosis but also because of the bearing they have on the evaluation of selected skin tests which may be carried out in such cases For if the eruption is of the hyperacute variety as in poison ivy dermatitis deliberate clinical re-exposure or a patch test with the allergenic material would be expected to produce a very strong papulovesicular response If on the other hand the eruption clinically consists only of a mild erythema or a noninflammatory thickened patch it would be unwarranted to expect an intense skin reaction on deliberate clinical re-exposure or from patch tests with the causative agent.

Itching may be absent or vary in intensity from very mild to such severity as to be incapacitating Burning and stinging may be present and on occasion when there is marked edema or fissuring patients may complain of pain

n deliberate sensitization to 2·4 dinitrochlorobenzene, about 20% of all subjects who by having a spontaneous flare-up phenomenon give evidence that they have become allergically sensitized, lose this sensitivity spontaneously within a few weeks. Moreover while the information available from various studies is not consistent, it would appear that loss of contact sensitivity within a few years after an allergic eczematous dermatitis is not unusual. It seems that the incidence of the loss of sensitivity varies with different allergens and in different parts of the world. Surprisingly enough the in adequate evidence thus far available suggests that very marked changes in the level of sensit vity to eczematogenic allergens can occur i dependently of the mount and frequency of intercurrent exposures to the particular allergen a d conversely that sensitivity persists—as has been known for many years—in the apparent absence of re-exposure.

The question as to what produces continued allergic sensitivity in the bsence of known exposure is not much nearer solution today than when first asked many years ago Is the persistence due to allergenic material which remains in the reticuloendothelial system even if only in minute quant ties? This possibility cannot be abandoned in view of the recent findings in animal studies that allergenic materials can be stored in the reticuloendothelial system for a remarkably long time Does one allergenic exposure set up a more or less permanent change in antibody synthesizing enzyme systems I t exposure to immunologically related chemical compounds which on the basis of cross-allergenicity maintains allergic sensitivity for many years? Or does aller gic sensitivity persist even in the absence of the allergen itself, because of continued production of relatively large quantities of an antibody which, prior to allergic sensitiza tion, existed only i minute quantities as one of many nat urally occurri g antibodies?

No matter what the correct explanation may be t fact that fluctuations n the level of skin sen itivity do occur Some of these fluctuations are undoubtedly due to renewed exposures or to prolonged lack of exposures. For example in some instances even th small amount of allergen encoun tered in a patch test may be sufficient to change the level of exist g sen itiv ty The not infrequent flare up of an acute

period is dependent to some extent on the quantity of allergen encountered in the original sensitizing exposure. No matter how large the exposure however 5 days is the minimum period required for the full development of allergic eczematous sensitization

In allergic eczematous contact dermatitis the *spontaneous flare up phenomenon* accounts for some of the important clinical events which are known to occur This phenomenon is often seen following deliberate experimental sensitization to simple chemical compounds It is characterized by an eczematous eruption which appears following the initial sensitizing exposure and after an incubation period of sensitization but without additional subsequent exposure to the offending allergen This is explained by the trace amounts of allergen which persist on or in the skin from the time of the original sensitizing exposure yet cause no clinically visible cutaneous reaction until after allergic sensitization has fully developed The nature of this phenomenon clearly implies the fact that for each sensitization a spontaneous flare up can occur only once.

Once allergic eczematous sensitivity has developed the allergically sensitive skin as a rule regularly reacts on adequate re-exposure after a fairly constant period This period which is 24 to 48 hours with the outer limits being 12 to 96 hours represents the time lapsed between exposure of the sensitive skin to the allergenic substance and the appearance of the clinically visible eczematous response and has been named the *reaction time*

Once eczematous sensitization to a given allergen has been established the question arises as to the *persistence* of the *sensitivity* Formerly it was the general impression that once allergic eczematous contact sensitivity had been established, it ordinarily persisted for many years although the *degree* of sensitivity gradually diminished (usually after middle age) In recent years however increasing evidence has been reported which would lead one to assume that allergic eczematous contact sensitivity does not always persist over a period of many years. Early loss of sensitivity according to these reports apparently occurs in a not inconsiderable number of cases This, of course is of the greatest practical and medicolegal importance It has been shown for example that

ably also by the mononuclear cells themselves to the skin. When the supply of antibodies carried by these mononuclear cells to the skin ceases, the skin loses its sensitivity

Another piece of evidence in favor of the participation of the mononuclear cells in the allergic eczematous contact process s the great number of lymphocytes and monocytes surrounding the superficial blood vessels and n the blister fluid of all rgic eczematous contact reactions in contrast to the polymorphonuclear leukocytes wh ch predominate in the blister flu d of primary irritant reactions.

As is well known, once allergic sensitization has becom established following the exposure of even a very small area of skin to a specific allergen the entire ntegument is as a rule capable of reacting when exposed. When, however one area after another of eczematous dermatitis appears at interval of 1 or more days up to as long as 3 weeks after the xposure to the responsible allergen and there are no known e-expos res, other explanations are, of course, necessary There may ha e been hidden exposures to the responsible allergen as from clothing garden utensils, tools, the sk n or hairs of pets and other animals and the like which may remain ontam nated with such allergens as poison i y insec ticide sprays et for amazingly long periods.

Another explanation may be a sudden or gradual ncrease in the degree of skin sens ti ty due to the very recent ex posure t the offending allergen In this connection one must realize that the occurrence of a clinically visible reaction n allergi sk n depends among others on two factors namely the quantity of allergen deposited per skin area and the degree f sen tivity of that particular area. For example if previously sensitized skin was exposed to the esponsible allergenic material so that different sites received different quant ties of allergen varying from traces to relatively large amou t and assuming that the existing level of sensiti ty for that material was the same fo all of the skin, then those sites ha ing the heaviest deposits of allergen would be ex pected to respond first with an eczematou eruption Thereafter when the general level of skin sensit vity had been gn fica tly boosted due to the exposure to the responsible allergen, those sites which previously had received the maller quantities of allergen and had failed to de elop an

dermatitis following such a small exposure bears witness to this Perhaps these are anamnestic responses and reactions similar to those which occur in other immunologic states It must be realized however that such fluctuations in sensitivity are not necessarily the result of chance or deliberate exposures to the allergen or to immunologically related substances but that certain *nonspecific factors* within the patient such as his hormonal status circulating or tissue proteins enzyme systems diet etc. may well have an important bearing on the demonstrable level of sensitivity from one time to another

Among other unresolved problems of clinical and theoretical importance is the mechanism by which allergic sensitivity spreads from the sites of original exposure to involve the entire skin surface Numerous experiments have been done in an effort to elucidate the question of exactly how sensitization proceeds and while as yet none has supplied a final answer the weight of evidence at present is against the spread of the sensitization by way of the skin itself from the site of the sensitizing exposure Previous experimental work as well as beautiful recent studies clearly demonstrate that in order for sensitization to occur adequate quantities of (conjugated) allergenic material must be carried to the regional lymph nodes and therefore the lymphatic pathways between skin and regional lymph nodes as well a the regional lymph node itself must be intact The role of the nervous system has been inadequately investigated to date if any even tentative inferences can be drawn from the results available thus far it is that the nervous system does not play an important role in allergic eczematous sensitization

Based on the experimental findings that lymphocytes and monocytes do carry antibodies in guinea pigs sensitized by exposure to contact allergens attempt have been made to duplicate these findings in man However efforts in man to demonstrate antibodies" associated with allergic eczematous contact dermatitis hitherto had been generall considered fruitless until very recently when antibody demonstration has been reported through passive transfer with blister fluid white cell suspensions and blood transfusion According to this theory mononuclear cells carry the antibodies produced in the reticuloendothelial system and prob

As a matter of fact, the number of substances which may cause allergic eczematous contact dermatitis is so great that when this type of eruption is suspected, the physician must be suspicious of not only the common but also of the uncommon and sometimes most bizarre of contacted substances. Allergic eczematous sensitization may be produced by agents ranging from simple chemical ions such as nickel iodine, etc., to relatively simple organic and inorganic chemical substances, to substances with complex large molecules whether occurring in nature (such as proteins) or synthesized by man in the laboratory.

Some of the features which tend to lend allergenic sensitizing capacity to particular chemical groupings have been elucidated in the past. In general it can be said that the potential to engender allergic eczematous sensitization appears to be related to the capacity of substances to enter into reactions with certain constituents of the skin especially proteins, and constituents of proteins, i.e. their ability to conjugate. In years past it had been assumed that the eczematogenic allergen itself, acting as a hapten (partial antigen) immunologically was the sole factor determining the immunologic specificity of the combination of the allergenic compound with certain skin constituents. It was believed that the large molecular substances derived from the skin (e.g. proteins) played no role in the specificity of the reaction simply serving as nonspecific carriers (Schleppers) in the newly formed complex. In recent years, however some investigators have felt that a part of the specific activity of the complex may well be dependent on certain characteristics of the very same large molecular part.

In order to compare the relative sensitizing capacity of the many potential sensitizers there has been established the concept of the *sensitizing index* of a substance and the means for ascertaining these indices. The sensitizing index is the relative capacity of a given agent as compared with other agents to engender sensitization in a group of human beings or animals. This must be sharply differentiated from the *index of sensitivity* which is the incidence of a population's previously acquired sensitivity to a given agent. For obvious reasons, it is impossible to establish the sensitizing capacity for large numbers of eczematogenic allergens. Often it is not

eruption could now be expected to show an eczematous response

In rare instances only a limited area of skin appears to acquire or retain the allergic hypersensitivity so that clinical or patch test exposure elicits a reaction only in those limited areas and not in other parts of the integument In these exceptional instances it is essential of course that re-exposure or patch tests take place on the affected areas since otherwise erroneous conclusions including unjust medicolegal judgments may result More frequent is the occurrence of greater sensitivity of one or more skin areas than of the rest of the integument In such cases these particular areas may flare up on exposure of a distant site without the more sensitive areas themselves having external contact with the allergen in any detectable manner It would appear that the commonly observed flare-ups of affected areas which follow patch tests done with the causal allergen during the acute phase of the eruption belong in this category

The previously outlined current theory regarding the mechanism by which the skin cells maintain their sensitivity is inadequate by itself to explain the phenomena of entirely localized sensitivity or of localized sensitivity which is much greater at one site than of all the remaining skin In order to account for these phenomena one would have to call on auxiliary theories such as those which assume that some skin cells have a greater capacity to take up or fix antibodies than others or that some skin cells lack the capacity to take up or fix antibodies or that there are significant anatomic differences between various skin sites It is obvious that very much remains to be learned in this highly important segment of dermato-immunology

For the sake of completeness it is worth stressing once more the now well known fact that the blister fluid in cases of allergic eczematous contact type dermatitis is not allergenic and that therefore it cannot cause new lesions elsewhere on the patient s skin nor on the skin of other persons

Nature of Allergens

As was previously pointed out there is hardly a substance which cannot prove allergenic to some one or more persons.

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pounds (secondary allergens) The mechan m of cross-sensitization has been discussed in much detail elsewhere. Suffice it here to state that it occurs between immunochem ically closely related substances or where two or more previously unrelated compounds through conversion in human tissues are broken down into products which are immunochemically related.

It should be noted for example that in one instance benzocaine may be the primary allergen producing the original allergic sensitivity with cross-sensitization to the secondary allergens procaine, paraphenylenediamine and para aminobenzoic acid wh le in another case paraphenyl enediamine may act as the primary allergen with cross sensitization dermatitis due to the secondary allergens ben zoca ne, procaine and para-aminobenzoic acid. It is of clinical mportance to recognize that the more intense the degree of hypersensitivity and the more frequent the oppor tu ity for exposure to the primary allergen the greater appears to be the tendency to the development f cross-sensitization to additional substances.

The allergen c compo ent respon ble for cross sensitization just as previously pointed out for the primary sensitization, may vary in si e from very small to qu te large chemical units. Examples are elements such as mercury nickel and iodine or simple groupings of molecules, as the amino group n the para position of the benzene ring or a side chain w th a tertiary amine as found in some of the topical anesthetics, or in some instances large molecular structures as the polysaccharides in certain species of fungi.

One f th highly mportant practical consequences of cross-sensitization is that it enables compounds, which themsel es generally lack the capacity to produce allergic eczematous sensitization to elicit severe allergic reactions in skin previously sensitized by a hemically related substance of high sensitizing capacity

While there are many examples of cross-sensitization in eczematous allergic eruptions in human beings we shall mention only a few which are of considerable practical importance. Frequently encountered instances of cross-sen itization for example, are found among a group of com-

very difficult however to establish the relative sensitizing capacities of two or more substances in man or experimental animals

At times it may be advisable to establish the index of sensitivity to a group of substances among a given group of persons It should be noted that such data always are based on a particular group of subjects tested at a particular time and that the findings do not necessarily apply to other groups. Such a study was done some time ago among selected patients attending the New York Skin and Cancer Unit. Patch tests done with a series of commonly used topical therapeutic agents yielded the following data no existing allergic hypersensitivity was found to benzoic acid benzyl benzoate and ichthammol Allergic hypersensitivity was found to exist in less than 2% of patients to boric acid aluminum acetate menthol naftalan petrolatum and phenol in from 2 to 5% of patients to oxycholesterol petrolatum ointment (aquaphor) hydrous wool fat dibucaine (Nupercaine*) resorcinol salicylic acid and Vioform* (iodochlorhydroxyquinoline) and in more than 5% of patients to ammoniated mercury ethylaminobenzoate (benzocaine) red mercuric sulfide crude coal tar coal tar solution juniper tar tetracaine Pragmatar* (containing cetyl alcohol-coal tar distillate near colloidal sulfur and salicylic acid) and chlorhydroxyquinoline compound ointment and benzoic acid and salicylic acid ointment NF

Of course there are many other topical therapeutic agents which have shown signs of being potent allergenic sensitizers and which were not included in the above series Among them to mention only a few are butesin picrate and many other local anesthetics Furacin* sulfathiazole chlorpromazine Thephorin* Phenergan* and some other antihistamines

Cross-Sensitization

An increasingly important aspect of allergic eczematous contact dermatitis is cross-sensitization i e the phenomenon where allergic sensitization of human skin produced by one compound (the primary allergen) is associated with eczematous allergic sensitization to one or more other com

pounds (secondary allergens) The mechanism of cross sensitization has been discussed in much deta l el ewhere Suffice t here to state that it occurs between immunochemically closely related substances or where two or more previously unrelated compounds through conversion in human tissues are broken down into products which are immunochemically r lated.

It should be noted for example that in one instance benzocaine may be the primary allergen producing tl e original allergic sensit vity with cross-sensitization to the secondary allergens procaine, paraphenylenediamine and para ammobenzoic acid while in another case paraphenylenediamine may act as the primary allergen with cross-sensitization dermatitis due to the secondary allergens benzocaine, procaine and para aminobenzoic acid. It is of clinical importance to recognize that the more intense the degree of hypersensitivity and the more frequent the oppor tu ity for exposure to the primary allergen the greater appears to be the tendency to the development of cross sensitization to additional substances

The allergenic component responsible for cross-sensitization just as previously pointed out for the primary sensitization may vary in ize from very small to quite large chemical units Examples are elements such as mercury nickel and iodine or simple groupings of molecules, as the ammo group in the para position of the benzene *ring* or a side chain with a tertiary amine as found in some of the topical anesthetics or in some instances large molecular tructures as the polysaccharides in ertain species of fu gi

One of the highly important practical consequences of cross-sensit zation is that t enables compounds, which themselves generally lack the capacity to produce allergic eczematous sensitization, to elicit severe allergic reactions n skin previously sensitized by a chemically related substan e of high sensitizing capacity

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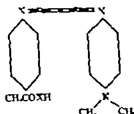
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should be aware of the fact that cross-sensitization to para aminobenzoic acid and its esters can occur after primary sensitization to procaine, sulfonamides paraphenylenediamine, etc A practical consequence of this fact appears to be that the manufacturer of a commonly used sunburn prevention cream recently has replaced the para aminobenzoic acid ester with a chemically unrelated sun filtering agent apparently because of the increasing incidence of allergic reactions to the para-aminobenzoic acid ester It may be worth mentioning here that the phenomenon of cross-sensitization may well play a role also in photoallergic eczematous reactions



An azodye used in coloring Nylon stockings

to para aminobenzoic acid which are now receiving increasing attention.

Azodyes which are used for many purposes and are encountered daily by millions of persons in general possess a very low sensitizing capacity Examples are those used in clothing cosmetics, drugs, leathers foods and beverages and gasolines. The cutaneous eruptions which they cause are usually the result of their role only as secondary allergens, the primary allergens being such potent related allergens as benzocain paraphenylenediamine, sulfonamides etc.

More recently cross-sensitization has been shown to occur between compounds containing the pyridine ring such as pyribenzamine and sulfapyridine.

Phenergan used locally must be recognized as a frequent sensitizer with many types of cross-sensitization. For example 30% of patients shown to be allergic to Phenergan[9] were also sensitive to paraphenylenediamine. Though rare cross-sensitization between pyribenzamine and Phenergan has been reported.

Clinically highly important is the fact that there is a high

monly used agents which chemically are aromatic amines as well as among chemically related compounds.

Examples are

H_2N–C₆H₄–NH (Paraphenylenediamine)

H_2N–C₆H₄–C(=O)–O–C_2H_5 (Benzocaine)

H_2N–C₆H₄–C(=O)–O–C_2H_4–N<(C_2H_5)(C_2H_5) (Procaine)

H_2N–C₆H₄–S(=O)(=O)–NH_2 (Sulfanilamide)

It is of practical importance to realize that sensitization to one of the above compounds does not mean necessarily that the patient will become allergic to any or many or all of the chemically related compounds

While the topical use of sulfonamides is now the exception rather than the rule in the United States this group of drugs is still frequently administered systemically and is occasionally used for local applications. Moreover the carbonic anhydrase inhibitor Diamox® (which is now widely used in glaucoma and edema due to congestive heart failure) and certain new compounds which have an antidiabetic effect on oral administration are all sulfonamides Although they are only distantly chemically related to the other sulfonamide drugs they must be considered with respect to cross sensitization

H_3C CO NHC(N=N)(S)C SO_2 NH_2

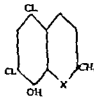
5-Acetamido 1 3 4 Thiadiazole 2 Sulfonamide Acetazolamide (Diamox®)

When sensitization to one sulfonamide is known to exist cross-sensitization to other sulfonamides can occur as well as cross sensitization to certain of the topical anesthetic paraphenylenediamine and para aminobenzoic acid etc

While clinical incidence of allergic sensitization to para aminobenzoic acid as a primary allergen is very low one



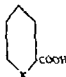
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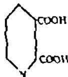
[illegible]



[illegible]



[illegible] Acid
([illegible] acid)



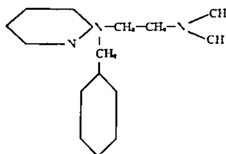
[illegible] Acid
([illegible] 2, 3 [illegible] acid)

adhesive tape in the United States is apparently very low it is still sufficiently important to prompt the physician to be on the lookout for possible cross-sensitization reactions. The mild reactions which are commonly caused by adhesive tape are generally recognized as being due to primary irritant and other nonallergenic effects. Allergic sensitivity to adhesive tape and its ingredients has been well studied in the past and it has been known that most adhesive masses contain natural rubber, zinc oxide and coniferous resins and other substances. Recently it has been pointed out that while any one of the many components of adhesive tape may be responsible for allergic sensitization, such reactions are most often caused by resins and turpentine, and somewhat less by rubber which itself contains many substances as adjuvants antioxidants and plasticizers.

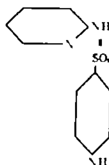
When sensitization to rubber exists, it has been considered *theoretically* possible that cross-sensitization to other acyclic terpenes may occur including such materials as gutta-percha and possibly essences of lavender and geranium, coloring as saffron and certain cosmetic preparations perfumed with citrus extracts.

(37%) incidence of cross-sensitivity between Phenergan® and chlorpromazine.

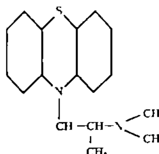
When allergic hypersensitivity to iodochlorhydroxyquinoline (Vioform®) is manifest, one can also anticipate sensitivity to diiodohydroxyquinoline (Diodoquin®) and chlor-



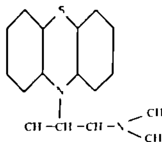
Pyribenzamine



Sulfapyridine



Phenergan®



Chlorpromazine

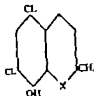
hydroxyquinaldine (Sterosan®) although this is not always the case. On the other hand, this group sensitization is not ordinarily carried over to certain mixed chlorhydroxyquinolines (Quinolor® compound).

It is believed that the actual allergenic complex of the halogenated hydroxyquinolines are the carboxylated pyridines (picolinic and quinolinic acid) to which they are changed and which also have been known to produce positive patch test responses.

While the incidence of allergic eczematous sensitivity to



[illegible] ([illegible] [illegible] hydroxyquin[illegible])



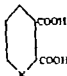
[illegible] ([illegible] hydroxyquin[illegible])



[illegible] (1, 7-[illegible] [illegible])



[illegible] Acid ([illegible] acid)



[illegible] Acid (pyridine 2, 3 [illegible] acid)

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Of course, patients with sensitization to turpentine and terpenic resins must be cautioned about exposure to the many preparations which contain these substances such as paints varnishes etc.

An example of cross sensitization which is of some practical interest is that between tetramethylthiuramdisulfide the germicidal agent in a new soap and thiuram compounds present as antioxidants in some rubber articles including rubber gloves The very few allergic reactions which have been seen after use of the new soap always appeared to be secondary to previous primary sensitization engendered by the thiuram compounds added to the rubber articles during their manufacture.

Numerous examples of cross sensitization are known to occur also among the plants e g those of the rhus anacardiaceae group including poison ivy poison oak poison sumac, Japanese lacquer mango cashew nut shell oil etc. Also of practical importance in this category is cross-sensitization between the oleoresins of iris (from which the insecticide pyrethrum is prepared) ragweed and chrysanthemum

Another category of group reactions is that seen for various tars such as crude coal tar wood tars shale oil tars and bituminous tars and their derivatives and extracts as used for topical therapy It is not surprising to see an individual who is not only allergic to crude coal tar but also to some or many of its refined forms and extracts as liquor carbonis detergens bleached and water soluble fractions etc. Because of cross sensitization, however this sensitivity can but does not necessarily extend to the other varieties of tars mentioned

It should be noted that in the examples of cross sensitization just discussed the multiple *sensitizations are* always based on specific allergic processes. These must be differentiated from certain nonspecific polyvalent sensitivities which are known to occur in individuals with highly acute and spreading eruptions Furthermore, apparent cross sensitization reactions sometimes have been shown to be due to contamination. For example, where allergic hypersensitivity to both nickel and cobalt has been demonstrated it is difficult, if not impossible to be certain that either the co-

balt or the nickel are pure substance and that they do not contain trace amounts of the other metal.

An interesting finding is also where cross-sensitization exists to substance B following primary sensitization to substance A but does not occur to substance A following primary sensitization to substance B. This may be exemplified by the sensitivity to paraphenylenediamine which has been shown to occur in 30% of subjects developing allergic hypersensitivity to Phenergan.* The reverse however is *not* true: subjects known to be allergic to paraphenylenediamine have *not* been shown to possess an allergic sensitivity to Phenergan. This apparent paradox is explained by the chemical events which are thought to take place: that is, that the complex Phenergan structure is broken down to become the simpler paraphenylenediamine structure or one closely related. To the contrary, it is not believed that the simpler paraphenylenediamine structure can be built up to any compound even closely resembling the more complex Phenergan* formula. Another example has been reported with respect to sulfonamides. Subjects with primary sensitization to sulfonamides are said to cross-react to paraphenylenediamine and to chemically related synthetic anesthetics in 100% of cases. On the other hand, subjects with primary sensitization to local anesthetics cross-react with paraphenylenediamine in 90% of cases and those with primary sensitization to paraphenylenediamine cross-react to local anesthetics only in slightly less than 20% of cases.

Nonspecific Factors Influencing Allergic Eczematous Contact Sensitization

Exposure to a potential sensitizing substance often is not the sole factor determining the occurrence of allergic eczematous contact dermatitis. Proof of this rests with the clinical evidence that many persons do not become sensitized even to such potent allergenic compounds as 2,4-dinitrochlorobenzene and that only an *exceedingly small* percentage of the population become sensitized to such commonly and frequently used items as cosmetics, including lipstick, creams, powders, fingernail polish, deodorants, etc.; clothing including natural fibers as wool, cotton, camel's hair

and synthetic fibers as nylon rayon and other acetates leather as in gloves shoes and so on ad infinitum

There are many obviously nonspecific factors which help to establish allergic eczematous sensitization These factors probably act by any number of mechanisms some locally from without others from within via systemic pathways One might conceive of these nonspecific factors contributing to the production of allergic eczematous dermatitis in the same sense as a *catalyst contributes to a chemical reaction* their presence appears to be necessary but they do not actively take part in the immunologic phase of the reaction. Moreover even when allergic eczematou sensitization to a specific substance has fully developed allergic eczematous contact dermatitis does not necessarily develop on each and every exposure or in all exposed skin areas. On the contrary there are excellent examples showing that in some patient even with existing allergic sensitization even very definite *clinical exposure does not necessarily produce dermatitis in* the exposed sites Dermatitis due to dyes in stockings is a pertinent example in most patients developing a dermatitis from such dyes it is usually present only on the dorsa of the feet and in the popliteal spaces although the entire foot leg and part of the thigh are also exposed to the allergenic stocking

The principal factors which determine man s susceptibility to sensitization are to a large measure inadequately understood It can be stated with reasonable certainty that heredity doe not play a clear-cut or unequivocal role in man in pa s ing along susceptibility to allergic eczematou sensitization However in guinea pigs it has been possible to deliberately breed strains with relatively high susceptibility to contact sensitization

The following are among the non pecific factor which alone or in combination are believed to contribute to the development of allergic ensitization to a given allergen or to the occurrence of dermatitis in *already sen itized pers n*

1 Simple pressure making for more intimate contact f the allergen with the skin

2. Friction enhancing the opportunity for contact and f r *penetration* and in addition tending to remove some of the protective structures and material from the skin s urface

3 Sweat other secretions and wet work probably ai l in

sens tization by producing maceration an l also by acting to solubilize ionize and extract certain allergenic material and thus bring larger quantities of allergen in more intimate con tact with the skin

4 Nonspecific irritation of the skin as well a burning maceration and inflammation due to physical factors or chem ical For exampl the capacity of normal human skin to undergo eczematous sensitization to certain allergen has been hown to be more than doubled if the allergen is appl ed at the site of a chemical or thermal burn.

It is not clear how these factors act to increase man s susceptibility to sensitization or to enhance the elicitation of a dermatitis. There are many possible mechanisms which have been considered n order to explain how these non pecific factors act to aid in the development of allergic eczematous sensitization They help to make a ailable relati ely large quantities of tissue components suitable for conjugation with simpl chemical they attract cells including mononuclear ell and macrophages which are believed to play a role in sen tization they cause a h ft of th local skin pH toward the alkaline side they ncrease permeability and therefore augment penetration of certa n ubstances nto the skin and perhaps also facilitate the allergen s reachi g the local lymph nodes In uch altered kin, nfectious m cro-organisms are more likely to be p esent, a factor which n turn might facilitate sensitization or the production of dermatitis as has been suggested by experimental work n the past. The role of the localized acanthosis which may be produced by these factors also must be gi en serious c nsideration, n e t has been shown n gu nea p g that skin sites which deliberately have been mad acanthot c have n ncreased suscept b lity to re ct with eczema like changes following applicat on of an allergen

5 A hift f the normally acid skin pH toward the alkaline side (di turbed alkali neutralizi g capacity) as is often caused by prolonged exposure to soaps and other alkalin cleansers.

6. A di turbed acid neutralizing capacity

Among ther features which hav been considered with respect to their influence on allergic sensitization are exces i grea mess of the skin through which contact with fat sol bl allergens is ncreased, excessi formation of keratin

favoring sensitization to substances such as dyes which readily combine with keratin and lack of adequate keratin layer permitting excessive penetration of allergens into the skin

In addition to these there are undoubtedly many other contributing factors which cause alterations in susceptibility to allergic eczematous dermatitis from time to time from one skin site to another and from one person to another Mention has already been made of cross-sensitization and of nonspecific polyvalent sensitization in which there is the possibility of reactions to exposures which under ordinary circumstances would not be troublesome.

Experience has shown that individuals having atopic dermatitis as a group do not have greater than normal capacity to develop allergic *eczematous* sensitivities.

Among the systemic factors which influence susceptibility to eczematous sensitization in nonsensitive subjects and to the occurrence of allergic eczematous contact dermatitis in already sensitized individuals the role of the adrenal hormones has attracted increasing attention. To date there is no reliable evidence that the administration of corticosteroids or ACTH in man interferes with the establishment of such sensitization. It has been shown however that often there is a slight decrease in the level of an existing sensitivity when *adequate* doses of these hormones are given systemically i e. that there may be a quantitative shift causing previously positive reactions to patch tests with *highly diluted* allergens to become negative The quantitative reduction in degree of sensitivity which was noted was not sufficiently pronounced to cause negative reactions in patch tests with *standard* dilutions of allergens As yet we have not observed a single case in which complete abolishment of existing eczematous allergic sensitivity has occurred due to therapy with ACTH or cortisone or related substances although such an occurrence has been reported.

PRINCIPAL STEPS IN ESTABLISHING A DIAGNOSIS OF ALLERGIC ECZEMATOUS CONTACT DERMATITIS

Differential Diagnosis

When confronted with eczematous lesions whether single or multiple isolated or scattered patchy or generalized the

differential diagnostic possibility of an allergic eczemat u contact dermatitis always must be borne in mind. On the other hand, of course it would be entirely nonsen ical t n estigate and manage an eruption as an allergic eczematous contact dermatitis unless the clinical features uggest this particular ariety of eczema and exclude the many other varieties f eczema which can resemble m re or les closel the allergic form.

Thi is not the place for a detailed discussion or cor ation of the differential diagnosis of eczematous and f other cutaneous diseases which might be with allergic eczematous contact dermatitis. Su present a b no means complete listing of those which we ha e seen mistakenly diagnosed as al' atous contact dermatitis (1) eczematou les primary irritants phy ical agents (2) n 3 primary fungous eruptions (4) ther id type eaction (5) atopic (ther dermatitis, (7) psoriasis especially se tized lesions (8) infectious eczematoid pu tular eruptions of the hands and feet of n pustular "bacterids" and pustular eruptions (11) herpes simplex, especially common localizations (12) dermatitis distinctive exudative discoid and l sis (14) erythrodermas based on causes togenic allergens (15) erythema m etc.

The term allergic eczematous ludes those ruptions which are based tou sensitization but which are the eczematogenic allergen from those resulting from exposure u contact-*type* dermatitis, the allergen l mphatic and hematogenous tes of internal e posure, be it by gestion, or by absorption tl ral vaginal or rectal the nly difference between dermat tis is the avenue of t ontact-*type* and contact

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Th term llergic eczematous contact-*type* dermatitis includes those eruptions wh ch are based on an allergic eczem atous sensitization but which are elicited by exposure to the eczematogenic allergen from within in addition to those resulting from exposure from without In allergic contact-*type* dermatitis the allergen is transported via the l mphatic and hematogenous routes to the skin from the sites of internal exposure, be it by injection, inhalat on, n gestion, or by absorption through the conjunctiva, nasal oral, aginal or rectal mucous membranes In principle then, the only d fference between allergic contact and contact-*type* dermatitis is the enue of exposure. The histologic p ctures of contact-*typ* and contact eczematous dermat tis are gen

erally identical In some cases there are however certain distinguishing clinical features. In contact-*type* eczematous dermatitis the eruption in general tends to be symmetrically distributed as in other hematogenously produced dermatoses Moreover it often involves especially areas previously affected with dermatitis due to the same agent and it tends to be widespread.

Ordinarily histologic examination of a tissue specimen is not required in order to arrive at the correct diagnosis in allergic eczematous contact dermatitis. In the exceptional cases where study of the histopathologic changes becomes necessary the following features may prove helpful for differentiating between eczematous eruptions caused by an allergic mechanism and by primary irritants

The following features favor an allergic eczematous eruption

1 In the epidermis—intercellular edema (spongiosis) and vesicle formation usually starting in the lower part of the prickle cell layer
2 In the dermis—edema and perivascular cellular infiltration predominantly with mononuclear cells
3 In the vesicle fluid—a considerable number of mononuclear cells

The following changes are more characteristic of a *primary irritant* eczematous reaction

1 In the epidermis—intercellular edema (spongiosis) and vesicle formation usually starting near the surface may show early erosion and necrosis
2 In the dermis—progression of necrosis perivascular reaction is variable
3 In the vesicle fluid—predominance of polymorphonuclear cells

Localization and Configuration of Lesions

In allergic eczematous contact dermatitis—in contrast to many other allergic cutaneous diseases—the topography of the presenting eruption often is the single most useful aid in identifying the offending allergen With certain exceptions it may be assumed that in almost every case the eruption starts and is most severe at the sites of principal expo-

sure no matter how widespread it may become later on. Therefore, it is absolutely essential that the investigator establish at the very beginning of his examination (no matter how diligently a scatterbrained, flighty or un-co-operative patient may attempt to deter him) the site or sites of onset and of principal involvement of the eruption. Thus a dermatitis of bandlike configuration across a man's forehead is almost always the result of some ingredient of the inside hat band. Localized roughly oval or round eczematous patches on the mid-thighs of a woman (particularly the posterior aspect) almost invariably are caused by nickel or other material in the clasp of the garter belt. An allergic eczematous contact dermatitis on the dorsa of the toes and feet usually is caused by some allergenic material in the shoes, socks or stockings.

It is probably no exaggeration to state that in many cases of allergic eczematous contact dermatitis identification of the offending allergen is possible even without a long and detailed history. This is accomplished by careful consideration of the localization of the eruption, provided the patient is seen *before* secondary factors, especially injudicious treatment, have befogged the clinical picture.

There are, however, some highly important exceptions to this rule. Certain parts of the human integument, such as the palms, soles and scalp, are notoriously more resistant to developing dermatitis to allergenic as well as nonallergenic exposures than the remainder of the skin. This does not mean that these regions do not participate in the allergic eczematous hypersensitivity, but it appears that much greater or more prolonged or intimate exposure to the allergen is necessary in order to produce a reaction. Therefore the palms, soles and scalp may fail to show involvement even though they may be the principal sites of exposure. In such cases the principal sites of *involvement* are likely to be the contiguous areas of the skin. Allergic eczematous contact dermatitis due to a scalp lotion is likely to affect not the scalp itself but mainly the forehead, eyelids, tops of the ears and adjacent pre- and postauricular areas and the nape of the neck. Dermatitis following squeezing of oranges is likely to affect, not the palms, but the interdigital webs and adjacent parts on the dorsa of the hands. Dermatitis due to an aller

genic foot powder dusted on the soles is likely to affect not the soles but the toe webs and the dorsa of the feet

Another circumstance where the site of major exposure is not the site of major involvement is where areas are relatively or entirely insensitive to the allergenic material. In this event, adjacent or even distant skin sites may be secondarily exposed by transfer of the allergen A pertinent example is nail polish applied to the insensitive nail. Only rarely does one see a dermatitis of the periungual skin or other parts of the hands which can be attributed to nail polish even in patients where at the same time the nail polish can be shown to be responsible for an eczematous eruption of such distant areas as the eyelids and sides of the cheek and neck which are contacted so frequently by the nails

Another example of this type involves the skin adjacent to mucous membranes For example allergic eczematous contact dermatitis of the inner thighs has followed the use of iodoform gauze packing of the vagina without any signs of involvement of the genital mucosa dermatitis of the lips and circumoral area has resulted from toothpaste containing penicillin without any signs of involvement on the oral mucosa eczematous eruptions of the skin of the perianal area have been seen as a result of the ingestion of poison ivy extract without any ill effects on the mucosal surface from mouth to anus. Numerous similar examples could be given and in each instance the particular mucous membranes whether vaginal oral or gastrointestinal usually remain free of any involvement whatsoever even following prolonged and repeated exposures In some patients however one sees coexisting allergic contact sensitivity of both the skin and mucous membranes to for example dental plates toothpaste lozenges etc

In the case of widespread eruptions an allergic eczematous contact etiology should be suspected if the areas which are protected from external exposure are not involved for example the intertriginous areas such as the axillae the groin the submammary region of pendulous breasts the folds of the upper eyelids and so on This rule of course does not hold when exposure to the eczematogenic allergen takes place via noncutaneous routes i e when one is dealing with an allergic eczematous contact type dermatitis For example

a patient who previously has acquired an allergic eczematous contact sensitization due to topical application of ammoni ated mercury ointment and who later on is gi en a dose of calomel by mouth or an injection of a mercurial diuretic may develop an eczematous erythroderma *without* sparing the kin folds.

Additional nd valuable aids in establish ng the diagnosis and discovering the etiologic factors of allergic eczematous contact dermatitis ar the arrangement and configuration of the skin lesions since to a large extent these will depend on the nature and shape of the allergen. A dermatitis wh ch is l near immediately suggests contact with a plant while walk ing through brushes or meadows or woods This does not mean that plant dermatitis cannot involve large areas w th out presenting l near lesions. The editors, for example on oc casion ha e seen very severe eruptions in bizarre arrangement involving principally the trunk, due to contact with the poison i y plant. Liquids which run from the site of application, uch as perfumes or after-shave lotions or deodorants usually tend toward ri ulet or finger l ke distr bution and treaks resembl ng the pendant from a necklace or hain Dermatitis due to topical medications which are applied to the hands or with the hands to other body areas hardly ver emains confined t the original areas of application but may affect any other part of the skin surface. Rather t quickly tends to in ol e not only the hands (usually not the palms!) but also egions frequently contacted by the hands ncluding the face (eyelids!) front and sides of the neck and, n men, the genitalia and in women the nner aspects of the th gh nea th ul a.

At times only the exposed" surfaces of the skin, i.e., those ordinarily not overed with cloth i g are invol ed with an eczematous dermatitis. In ch instances am ng other possibilities, one should consider an allergic etiology from an ir borne allergen. The localization of such eruptions due to ai borne substances is usually sharply confined to those ur faces (the skin which a e openly exposed, g the fa neck, \ of th neck and chest, hands, forearm and arms, thighs legs nd feet as the case may be Areas which are not regularly openly exposed, uch as the f lds of th upper ey lid and the fl xu of the elbows may be pared. The

distribution degree and type of involvement of exposed areas will also depend on the nature of the airborne allergen Pollens such as ragweed oleoresins are more likely to spare the *less openly exposed parts such as the inframandibular region* and the eruption is prone to be slow in onset and very chronic in course this may be attributed to continuous exposure to very small quantities of allergen during certain seasons On the other hand when the offending allergen is an *insecticide deodorant toilet water sprayed with an atomizer* or other airborne substance which is likely to be present in reasonably heavy concentrations very few exposed areas can be expected to be spared and the dermatitis will probably be quite acute *in* degree

In eruptions which are suspected of being caused by airborne allergens the possibility of a nonallergic dermatitis due to photosensitization will often have to be considered in *differential diagnosis In still other exceptional* cases a photosensitization process may be part of the mechanism producing an *allergic* eczematous dermatitis Examples of this type of "photo-allergy" are certain eruptions after the use of para aminobenzoic acid or one of its esters, followed by *exposure to the sun Unfortunately such joint synergistic* or additive mechanisms contributing to the production of allergic eczematous contact dermatitis did not always receive the attention which they deserved

It is not possible to describe even in outline form all the finer points and clues which in their aggregate and together with the necessary knowhow detective acumen and willingness to take the necessary time for careful questioning help one discover that a perianal dermatitis is the result of ingested mango or poison ivy extract rather than the local use of toilet paper or suppositories that a woman's facial dermatitis was caused by a tar ointment being used by her husband in the treatment of psoriasis rather than the more obvious recently *purchased glamour cream and that a man's* cheilitis resulted from a particular brand of lipstick used by his wife instead of from a new toothbrush or brand of toothpaste

Some Difficulties in Obtaining an Accurate History

It is not our intention to present a detailed outline which could serve as a guide for systematic questioning of patients

with suspected allergic eczematous contact dermatitis Rather we would like to ment on a few examples of difficulties as well as of errors or circumstances which in our experience have been the causes for failures in uncovering the etiologic agents in certain cases of this dermatosis.

In his search for causal allergens, the physician must always be alert first for the possibility that the dermatitis may be due to some allergen to which the patient previously had not been exposed. In some instances this may be a new material in that the patient previously was not exposed to it although it was not new in the sense of having been newly developed or synthesized. In other cases it may be an agent which previously did not exist. An example of this circumstance is the allergic eczematous reactions of the nail bed due to a new nail polish undercoat which were reported some years ago Patch tests done with the ingredients of the "undercoat showed that the artificial resins and rubbers that were included in this new product were responsible for the severe subungual and ungual changes which resulted from its use

On the other hand, one also should not overlook the possibility that an eczematous dermatitis may be due to a product which is so well known as to be thought "harmless and so widely used as to easily go unsuspected as being a possible causative allergen There is probably no better example of this than lanolin and lanolin derivatives, which despite their supposed innocuousness have been shown to be allergenic. It has been demonstrated that it is the mixed alcohols of wool fat, more specifically the fraction containing aliphatic alcohols, which are usually responsible for the allergenic activity of these products.

There are circumstances which may make it more than ordinarily difficult to find etiologic agents in some cases of allergic eczematous contact dermatitis. In exceptional patients certain mixtures of substances are necessary in order to produce the eruption, each component alone failing to elicit reaction An example is the patient who develops dermatitis only when using a particular cream and a particular powder simultaneously while no lesions whatsoever follow the use of one substance without the other In such a case negative patch test reactions must, of course, also be expected from the individual components while a positive

reaction would be expected to follow application of the mixture.

The single most important reason for failure to find etiologic agents is lack of time on the part of the investigating physician Even though the configuration of the lesions, their distribution and localization may provide valuable hints regarding possible causal factors it may still take many hours of repeated questioning to elicit the essential information Unfortunately this is not feasible in those clinics or private practices where relatively large numbers of patients have to be seen within a limited period.

Patients no matter how anxious to help the inquiring physician usually fail to remember important data regarding exposures they have had At the same time they fail to reveal exposures which while remembered erroneously are not considered important or relevant Repeated questioning during several visits often helps to educate the patient along lines necessary to correlate the offending exposure and the resulting dermatitis

Often neither physician nor patient is aware that a particular product which has been used and well tolerated for years without their knowledge may have been changed in composition by the manufacturer and that therefore actually a new exposure may have taken place Examples are the not infrequent changes in the ingredients of commonly used toilet articles such as toothpastes cosmetics etc topical proprietary medicaments household cleansers and so on

In our present world of ever increasing advances in the sciences and industry many different uses for chemicals old and new have been found and many new chemicals have been developed Their use is so widespread that it is improbable that one can go through a day without coming in contact with such substances What makes it extremely difficult for one to realize that such exposures are taking place is the hidden nature of many of these compounds e g coloring agents and preservatives in food antimildew agents and preservatives in leather plastics and resins in shoes artificial leathers synthetic cloths and other materials hormones germicides and perfumes added to cosmetics etc Actually we are in a new era one in which synthetic compounds are either replacing or are being combined with the older well

established items wood, paper cotton wool metal and other mineral plant and animal products.

The chemical advances have been just as rapid and as far reaching in the field of pharmaceuticals, so much so that this morning's catalog of available products is out of date this afternoon or more correctly that the catalog in press is complete before the ink is dry on the paper

Among the patients seen by the editors in private practice there are many who are taking some one or more of the new or newer drugs. And in addition to those medications which are prescribed by physicians, essentially all of the population are self medicating both externally and internally As a result of this trend, one must expect an increasing incidence of allergic eczematous contact and contact type dermatitis due to medications some of it perhaps based on cross sensitization

In addition to the many hidden and unexpected exposures already mentioned, there are the often unsuspected and at times bizarre forms of external contact with items such as clothing toilet articles, cosmetics etc., used or worn by other persons

No matter how intelligent or willing to co-operate the patient may be he generally fails to realize that even very infrequent or brief exposures to seemingly minute amounts of an offending allergen may be sufficient to cause or maintain an allergic eczematous contact dermatitis

These are but a few examples of the many problems which may be encountered in the attempt to discover etiologic allergen A detailed and properly recorded history is not only both time consuming and tedious, but very costly However it is often absolutely essential and well worth the effort and expense When one approach fails to uncover the offending allergen, repeated interrogations using other and different avenues of attack become necessary Obviously such questioning can never be complete until the etiologic agent has been unearthed.

(Part II of this article is planned for publication in a future YEAR BOOK.)

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I TREATMENT AND PREVENTION

A. Endocrine Therapy

Treatment of Systemic Lupus Erythematosus with Prednisone and Prednisolone, which have been found to be about four times as potent as cortisone and hydrocortisone in suppressing inflammatory manifestations of rheumatoid arthritis, was tried by Alfred Jay Bollet Stanton Segal and Joseph J Bunim (Nat'l Inst of Health) in 10 patients whose disease had not been satisfactorily controlled previously A typical facial rash of lupus erythematosus was present in two patients and a lesion resembling that seen in discoid lupus in another The initial suppressive daily dose was 20-60 mg (average, 35 mg) and the maintenance dose 5-30 mg (average 18 mg) Since administration of these two synthetic steroids in moderate doses does not cause sodium retention or edema, they offer important advantages over previously used steroids.

The authors found prednisone and prednisolone to be potent suppressive agents. They are capable of diminishing fever chills malaise anorexia, arthritis cough, pleuritic and precordial pain pleural and pericardial friction rubs, abdominal pain and tenderness, headache convulsive seizures, leukopenia, elevated sedimentation rate, and C reactive protein Renal abnormalities including proteinuria hematuria, cylindruria and azotemia, improved only when they had increased or appeared during an acute exacerbation of the disease, usually accompanied by fever and dehydration Serious renal disease was not influenced by these drugs. No significant alterations of blood pressure were observed. Edema was noted to diminish gradually during prednisone therapy Leukopenia improved in most instances, but anemia did not and alteration in serum albumin and globulin levels were only slight. The erythematous malar rash disappeared within two weeks in both patients and the chronic discoid rash improved gradually but had not entirely disappeared after three months of therapy The mucous membrane lesion consisting

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The most significant and disturbing side effect was severe diabetes mellitus in two patients who received the largest doses of these drugs In one, symptoms disappeared after transfer to hydrocortisone therapy and in the other insulin was used while prednisolone was continued.

Quantitative studies of the L.E. cells after treatment were done in 54 patients treated for at least two months. No cells were fou d in 23 and only a rare one i 8.

Since the incidence of spontaneous remission in sy tem c lupus erythematosus is 40% or more, Dubois does not start every patient on steroid therapy at o ce Bed rest and salicy lates to the point of intoxication are used. If there are cutaneou lesions or no response to more conservati e measures, antimalarials are used If the patient is seriously ill has renal or neurologi in ol ement o the illnes progres es, ster oids re gi en

► [The high incidence of peptic ulcers in this series of cases is particularly interesting and makes one wonder if persons with systemic lupus erythematosus (and ith rheumatoid arthritis as reported by Bunim) are mor prone to develop peptic ulcers than persons with various dermatoses who are being similarly treated with doses of prednisone or prednisolone considerably greater than 10 mg. daily—and for prolonged periods. In our ow experience the incidence of perforated peptic ulcers in patients with other dermatoses who have been treated with prednisone or prednisolone has been nil. W hav not done routine x-ray examinations of the upper stomach in search of -ray evidence of duodenal ulcers.—Eds]

Systemic Lupus Erythematosus Recent Advances in Its Diagnosis and Treatment are reviewed by Edmund L. Dubois[3] (Uni of Calif rnia, Los Angeles) in 160 patients with th disease. The pparently increasing incidence of the disease is a function of the more frequent use of the L.E. cell test well as of th perfection of more sensit e technics of L.E. cell detection

T tudy the fficiency of different L.E. tests, 63 simulta neon batteries f four L.E. cell tests were performed. These consisted of a sieved two hou clot, Snapper Nathan ri g technic a d se of 0.75 mg heparin/10 cc blood as an anti coagulant without rotation and with 30 minutes rotation with glass beads to traumatize the leukocytes (Z kham-Conley method) These studies comprised 47 proved cases of t eated and untreated ystemi lupus erythematosus 49.2% of the eved lots wer positi e, 23.8% f the plam heparin ized tests, 41.3% f th ring preparations and 54% of the

Am m Med 43 H August, 1954.

of shallow inflamed ulcerations present in three patients cleared within two weeks of therapy

Prednisone and prednisolone did not cause salt or water retention or hypopotassemia. Minor undesirable side effects were seen in all patients but it was not necessary to discontinue the drug in any

► [Experience with the use of these drugs has shown that they have but one advantage over hydrocortisone or cortisone, and that is the low incidence of sodium retention and edema. In all other ways they carry the same risks, except in degree, as hydrocortisone and cortisone

When we administer large doses of prednisone or prednisolone for more than short periods, we routinely prescribe potassium supplement in keeping with our own experience that they occasionally produce edema and potassium loss.—Eds.]

Prednisone and Prednisolone in Treatment of Systemic Lupus Erythematosus Edmund L. Dubois[2] (Univ of Southern California) treated 37 patients with active systemic lupus erythematosus with prednisone and prednisolone. The pattern of clinical improvement closely paralleled that obtained in previous work with corticotropin and cortisone Fever abated in 24-48 hours joint pains disappeared in several days and pleural effusions and cutaneous lesions subsided in 1 2 weeks Renal abnormalities of short duration often returned *to normal whereas those of long duration were unaffected by* this treatment.

In this disease prednisone appears five times as potent as cortisone and four times as potent as hydrocortisone on a *milligram for milligram basis. Prednisolone is five times* more effective than cortisone Using these figures the average well maintained patient may be transferred from treatment with older steroids to these agents The median main*tenance dose in this series was 22 mg /day of prednisone or* prednisolone. All patients receiving over 10 mg /day of either hormone must be placed on an ulcer regimen consisting of six feedings daily antacids and anticholinergic drugs to avoid the *22% incidence of peptic ulcer* that occurs in patients not on an ulcer regimen A low sodium diet is necessary for most patients taking over 50 mg /day of these hormone over long periods and for all patients with significant cardiac or renal disease to avoid edema and congestive failure

Side effects of these newer steroid were identical with those produced by the older ones but were lower in on et

(2) J A M A 161 427-433 June 2, 1956.

The most significant and disturbing side effect was severe diabetes mellitus in two patients who received the largest doses of these drugs In one symptoms disappeared after transfer to hydrocortisone therapy and in the other insulin was used while prednisolone was continued

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Since the incidence of spontaneous remission in systemic lupus erythematosus is 40% or more, Dubois does not start every patient on steroid therapy at once Bed rest and salicylates to the point of intoxication are used. If there are cutaneous lesions or no response to more conservative measures antimalarials are used If the patient is seriously ill, has renal or neurologic involvement or the illness progresses, steroids are given

► [The high incidence of peptic ulcers in this series of cases is particularly interesting and makes one wonder if persons with systemic lupus erythematosus (and with rheumatoid arthritis as reported by Bonum) are more prone to develop peptic ulcers than persons with various dermatoses who are being similarly treated with doses of prednisone or prednisolone considerably greater than 10 mg. daily—and for prolonged periods In our own experience the incidence of perforated peptic ulcers in patients with other dermatoses who have been treated with prednisone or prednisolone has been nil. W have not done routine x-ray examinations of the upper stomach in search of x-ray evidence of duodenal ulcers.—Eds.]

Systemic Lupus Erythematosus Recent Advances in Its Diagnosis and Treatment are reviewed by Edmund L. Dubois[3] (Univ of California Los Angeles) in 160 patients with the disease The apparently increasing incidence of the disease is a function of the more frequent use of the L.E. cell test as well as of the perfection of more sensitive technics of L.E. cell detection.

To study the efficiency of different L.E. tests, 63 simultaneous batteries of four L.E. cell tests were performed. These consisted of a sieved two hour clot, Snapper Nathan ring technic and use of 0.75 mg heparin/10 cc. blood as an anticoagulant, without rotation and with 30 min test rotation with glass beads to traumatize the leukocytes (Zimkham-Conley method) These studies comprised 47 proved cases of treated and untreated systemic lupus erythematosus 49.-% of the sieved clots were positive 23.8% of the plain heparinized tests, 41.3% of the ring preparations and 54% of the

[3] Ann Int Med 45 184, August, 1956

heparinized specimens rotated with glass beads. In three batteries the *sieved clot was the only positive test in five* the Zinkham Conley method and in two the ring technic The untreated heparinized method was never the only positive test in a battery and therefore has been discarded for routine use The number of L E cells and hematoxylin bodies was greatly augmented by the traumatizing technic It is advisable that at least three different types of L.E. cell tests be performed to screen a suspected case adequately Despite these refinements L.E. *cells are not found in all patients* with the disease

Of 163 patients 38 6% have had spontaneous remission before any special therapy Certainly many of the treated patients would have had remissions without such treatment At least two remissions were seen in 6% and three or more in 16% which makes evaluation of therapy difficult

Antimalarial drugs have a definite place in the treatment of systemic lupus erythematosus particularly in the milder cases. Their effect on the cutaneous lesions is almost specific. Arthritis is also greatly benefited Their synergistic use with steroids often reduces the steroid dose and may permit one to stop steroid treatment entirely Milder cases (80%) are benefited by antimalarials alone The optimal dose of these drug when used alone, is as follows atabrine* 100 mg three *times daily after meals If no improvement occurs within one* week the dose can be increased to as much as 600 mg daily chloroquine 0 5 Gm daily plaquenil* an analogue of chloroquine 800 mg daily

Steroid treatment is still the main tay of treatment in the acutely ill patient and benefits 90% of them In general steroids were started *with 300 mg/day of cortisone 240 mg* hydrocortisone or 40 mg/day of predni one or predni olone The steroids are increased within 24-48 hour depending on clinical results

Nitrogen mustard ameliorated the nephropathy of systemic lupus erythematosus particularly in more edemat u patients

The lives of these patients are prolonged by thi theraj y The median duration of life of 59 untreated or ina lequat ly treated patients was two years In the pre ent eries f 138 adequately treated patients ill for two year r m re le *than* 10% have died

► [The high incidence of spontaneous remissions (38.6%) of systemic lupus erythematosus as reported by Dubois is remarkable and it would be interesting to know the criteria on which the diagnosis was originally made in these particular cases.—Eds.]

Cortisone and Corticotropin Treatment of Pemphigus. Experience with 28 Cases over Period of Five Years is reported by Carl T. Nelson and Marvin Brodey[4] (Columbia Univ.). Twenty-seven patients had pemphigus vulgaris and one had pemphigus foliaceus. Twenty-one patients (75%) survived. All but two of these are able to pursue their daily activities without serious restrictions. One patient maintained clinical remission for 25 months without steroid therapy; the others required maintenance hormonal treatment in varying amounts. Originally, dosage ranged from 300 to 1,500 mg. or more/day in oral cortisone equivalents. In patients with severe disease, ACTH intravenously (25 mg. in 500-1,000 ml. of 5% dextrose in water given in six to eight hours) can be used to supplement oral cortisone treatment during first stages. Daily dosage required is the amount needed to prevent formation of new lesions and bring about clinical remission.

Two deaths resulted from major thromboembolic accidents during treatment. Five other patients who died probably received inadequate amounts of hormone treatment, judged by present standards. Aside from thromboembolic episodes, the most serious side effects of long term corticosteroid treatment were psychic disturbances, osteoporosis and reactivation of peptic ulcers.

Before ACTH and cortisone there was no consistently effective treatment for pemphigus. In such a relentless, highly fatal disease the aim of steroid therapy should be relief of distress and prolongation of life. Corticosteroid treatment must sometimes be undertaken as a calculated risk because of the existence of various complications. By observing certain precautions, it is often possible to relieve even the most severely incapacitated pemphigus patients. Continued hormone administration can then be planned with the hope that the disease may ultimately reach a natural remission which will permit withdrawal of steroids.

The percentage of survivors in this series greatly exceeds the expected survival rate with other forms of therapy. Although corticosteroid treatment is not completely satisfac-

(4) A.M.A. Arch. Dermat. 72:503, December, 1955.

tory and not without risk it seems reasonable to expect that results will improve as further experience with this therapy is gained

► [This article once more calls attention to the lifesaving potential of corticotropin and cortisone and its relatives in certain hitherto fatal skin diseases, of which pemphigus is the outstanding example. We would like to stress the importance of "hitting hard with an adequately high suppressive dose at the *very beginning* of therapy thereafter reducing the dose slowly and by small decrements. One should anticipate that therapy may necessarily have to be continued for years, and that only in a small number of cases may it be possible to discontinue it altogether —Eds.]

Some Aspects of Physiologic Effects of Cortisone in Treatment of Pemphigus Vulgaris in a patient treated for two years are reported by John Neill[5] (Glasgow)

Woman aged 54 with pemphigus vulgaris for 2½ years was treated with cortisone or ACTH for over 2 years. Diagnosis was confirmed by the intraepithelial site of the bullae and by acantholytic cells from the floor of the lesions. On a maintenance dose of 37½ mg cortisone daily and periodic courses of methylandrostenediol and potassium citrate she remained free from symptoms and complications.

The first course of hormone therapy was 100 units of ACTH for 13 days, 75 for 1 week 50 for 1 day and 25 for 3 days. She had partial remission of the skin condition, but severe crops of large bullae appeared around the eyes which became infected with an organism resistant to the usual antibiotics. When treatment was suspended on the 25th day relapse occurred at once. The 17 ketosteroid excretion rose and eosinophil count decreased during therapy but not to expected levels, indicating that the adrenal cortex was depressed.

Cortisone 150 mg daily completely eliminated the lesions. When 80 units of ACTH gel was substituted for one day local reactions occurred, and she had an immediate relapse After 24 hours, treatment was resumed with 100 mg cortisone and 40 units of water soluble ACTH Cortisone was stopped on the fourth day and 100 units of ACTH given alone. The skin condition cleared and she was maintained on 150 mg cortisone daily

A third course of 120 units of ACTH was substituted for 100 mg cortisone which had adequately stabilized the patient, but she had an immediate relapse which was controlled only by changing to 250 mg cortisone daily Before the change, 17 ketosteroid excretion was just above normal on the fourth day of ACTH below normal on the seventh day normal and only after cortisone was reinstituted did it increase markedly A fourth course of ACTH given when the maintenance dose of cortisone was 50 mg again resulted in immediate relapse which was controlled only after cortisone was resumed at 200 mg

As adrenocortical damage is likely to occur in pemphigus

(5) Brit. J Dermat 67 434-443, December 1955.

vulgaris, ACTH is unreliable as therapy. Adrenal depression due to cortisone is greater than generally realized and a sudden change from cortisone to ACTH may induce a relapse or, in long term cases, even adrenal failure. Thus a booster course of ACTH to maintain the integrity of the adrenal cortex is risky.

ACTH and cortisone differ in their actions, ACTH tending to produce excessive quantities of desoxycorticoids affecting salt and water metabolism, and cortisone tending to suppress these steroids. As ACTH is unreliable and substitution therapy is easier, cortisone, not ACTH, is the treatment of choice in pemphigus.

► [There are many views and opinions concerning the drug or drugs of choice and the correct method for their administration in pemphigus vulgaris. It has been demonstrated adequately that with corticosteroid or corticotropin, when used properly either alone or in combination, satisfactory results are usually achieved. Today there are two principal schools of thought concerning the periodic administration of ACTH during long term therapy with corticosteroids. One favors weekly, biweekly or monthly administration of ACTH for one or several days, while the other feels that the ACTH given in this manner is of little, if any, effect in stimulating an adrenal cortex which has been essentially put at rest by the corticosteroid.

It has been our experience that the periodic administration of ACTH ordinarily is not necessary during long term therapy with corticosteroids, provided the dose of the corticosteroid is reduced very slowly by small decrements over a prolonged period.

There are authorities today who believe that neither irreversible adrenal atrophy from corticosteroids nor hypertrophy from ACTH, of an irreversible degree, can occur.—Eds.]

Treatment of Erythroderma with ACTH and Cortisone is described by P. van Aken[4] (Univ. of Utrecht) with results in 10 patients. Three had primary erythroderma, in seven the condition was secondary to eczema. Three are now cured. One had a mild recurrence after suspension of hormone therapy and is now treated symptomatically with various salves. The general condition and that of the skin are fairly good. One patient discontinued treatment. Four of the other five are completely or practically symptom free on minimal maintenance therapy; one patient is still being treated in the clinic since the required maintenance dose of 150 mg. cortisone daily seems too high to warrant discharge.

Treatment is begun with 40 units of ACTH intramuscularly/day or 50-100 mg. cortisone. Dosage is increased rapidly to the effective amount, which is given until marked im-

(4) Nederl. tijdschr. geneesk. 95 :3256-3261, Oct. 29, 1951.

provement is evident The dose is then reduced gradually to the lowest possible amount on which the patient remains symptom free The maintenance dose differs in every case and must be adjusted from time to time in the same case The aim is to stop treatment completely but approximate duration of hormone therapy cannot be predicted accurately No more hormone is given than is strictly necessary and the significance of side effects must not be underestimated

The decision to treat erythroderma with cortical hormone requires careful consideration after thorough clinical and laboratory investigations Throughout treatment the patient must be carefully supervised

► [While the patient is receiving systemic ACTH or corticosteroids, every effort should be made to find effective topical medicaments. The regular use of external measures will at times make it possible to lower the dose of systemically administered steroid. Such combined therapy may have to be continued for a prolonged period until eventually the systemic drug can be discontinued while continuing the external applications.—Ed.]

Corticotherapy in Nicolas Favre Disease was inaugurated by P Quintin and J Duluc[7] (Saigon) Although the use of chlortetracycline proved to be a definite advantage in the treatment of this disease, results were occasionally incomplete and adenitis persisted in some cases Because of the anatomic pathologic characteristics of the lymphogranulomatous node with its reaction of exudative cells around necrotic foci and its tendency to develop into inflammatory sclerosis the authors believed corticotherapy to be indicated in lymphogranulomatosis inguinalis

In four cases cortisone and in one case metacortandracin were used with results which were superior even to those of chlortetracycline therapy because they were constant and fast Inflammatory changes began to disappear after two to three days and most were completely gone after eight days lymphangitis was seen to disappear after 24 hours Result were also complete no suppuration was observed and persistent adenitis was in the nature of a sequela The only relapse seen was due to the patient negligence and could be arrested promptly by continuation of the treatment When cortisone and antibiotics were given simultaneously results were equally successful Results were the same in acute and subacute cases and also in relapse The dose of cortisone

(7) Presse méd 64 1282, July 11 1956

required was less than 1 Gm. Metacortandracin had similar but less rapid effects.

► [These results suggest one more important indication for cortisone therapy. However, larger number of patients will have to be followed up for an adequate period before definite conclusions can be drawn as to the value of this treatment.—Eds.]

Adrenocorticotropin and Cortisone in Treatment of Severe Reiter's Syndrome is discussed by Donald T. Foxworthy, Robert M. Poske, Fran M. Barton, Lyle A. Baker and Max M. Montgomery (Chicago). Reiter's syndrome, a condition of undetermined etiology, is manifested by urethritis, conjunctivitis and arthritis, and in its moderate and severe form follows a characteristic course over a two to four month period. Remissions occur within a few weeks in the milder type of this syndrome. Patients with the severe form have persistent joint and muscle pain, high fever, rapid weight loss and marked joint effusions, and some also have extensive mucous membrane and skin lesions. They present a difficult problem in management since no specific therapy is available. None of the antibiotics modifies the course. The disease is self-limiting, but recurrences are not uncommon. Permanent joint damage rarely occurs.

The authors report 10 patients with Reiter's syndrome who were given ACTH or cortisone or both when symptoms were not controlled by analgesics and other conservative measures. All patients had arthritis, and all but two had urethritis and conjunctivitis. All but one had perimeatal erosions and balanitis circinata. The commonest skin lesion, observed in four patients, was keratodermia blennorrhagica. Duration of treatment and dosage necessary to control manifestations varied with individual patients. Total amounts given ranged from 0.475 to 9.58 Gm. and total treatment period from 11 to 87 days. Large suppressive doses should be given initially, the dose gradually reduced thereafter. Hydrocortisone was injected into the joints in several patients who had only one or two severely affected joints.

The authors found that ACTH and cortisone, when given in adequate doses for a long enough time, were effective in suppressing symptoms. The course of the disease was not shortened, however. Intra-articular injection of hydrocortisone was of value in the few instances in which it was used.

) Ann. Int. Med. 44:52-62, January 1956.

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The decision to treat erythroderma with cortical hormone requires careful consideration after thorough clinical and laboratory investigations. Throughout treatment the patient must be carefully supervised

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(7) Presse méd. 64 1292, July 11 1956.

gangrenosum, hemolytic streptococcic gangrene, progressive bacterial synergistic gangrene and necrotizing fasciitis. These ulcers have developed following surgical wounds, abrasions, contusions, lacerations, insect bites and gunshot wounds and have been associated with ulcerative colitis. Various treatments have been used, with at times only equivocal results; some authors have felt surgery only to be effective. Edwin T. Wright and Donald J. Greco (V.A. Hosp., Los Angeles) present a case in which hypogammaglobulinemia and pyoderma gangrenosum were successfully controlled with cortisone.

Man, 47 first noted two small "pimples" on the chest which developed into small ulcers. These gradually healed, leaving scars. Five months later several similar lesions developed on the chest which also ulcerated and healed slowly with scarring. One month later he was hospitalized with ulcerati lesions about 8-10 cm. in diameter on the right thigh and left buttock. The lesions had a necrotic base with a well demarcated, rolled, undermined, bluish red border.

The white blood cell count was 15,900 with a normal differential. The electrophoretic pattern showed low albumin and gamma globulin levels and increased beta fraction. Repeated cultures and smears consistently revealed alpha and beta hemolytic streptococci, nonhemolytic Staphylococcus aureus and albus coagulase-negative and hemolytic Staph. aureus coagulase-negative.

Treatment consisted of tyrothricin and bacitracin compresses on the ulcers and various antibiotic ointments applied locally. Penicillin, chlortetracycline, oxytetracycline and chloramphenicol were given parenterally. However the ulcers slowly enlarged and temperature remained elevated. Three days after 300 mg. cortisone daily was started, he became afebrile. The ulcers gradually became smaller and their base clean. After four weeks, healing was sufficient to allow skin grafting. When cortisone was discontinued, the grafts became infected and failed to take properly. When cortisone was resumed, fever subsided and the ulcers healed.

Electrophoretic determination after cortisone showed pattern similar to that before except that the gamma globulin level was further lowered.

It has been stated that cortisone may be of benefit by obtaining an antigen antibody reaction. In pyoderma gangrenosum a violent antigen-antibody reaction probably occurs; therefore cortisone is beneficial in that it decreases inflammatory response and may depress antibody formation.

► [Even though the authors refer to similar case which failed to respond to the administration of gamma globulin, it would have been inter

No complications of systemic or local treatment were observed. It is concluded that ACTH and cortisone, while not curative, are the most valuable agents available to control symptoms in severe forms of Reiter's syndrome.

Two Cases of Phagedena Geometrica (Brocq) Treated with Adrenocortical Hormones are presented by P. J. Hare (Univ. College Hosp., London). The cases were similar in that both patients, a man, 67, and woman, 50, had had chronic ulceration of the leg before onset of more recent and rapidly destructive ulcers elsewhere. Neither had had ulcerative colitis. The sequence of events was similar in both, starting with a boil-like lesion preceding the ulcers, which, although they extended laterally, seemed to remain skin deep without excessive destruction of deeper tissues. Bacteriologic results were inconclusive in both; no anaerobic organisms were recovered. The histology suggested an inflammatory process rather than gangrene due to vascular disturbance. The response to adequate doses of ACTH seemed undeniable, for healing had not occurred in either case with extensive treatment before use of the hormone.

The experience with these patients does not confirm the theory that the ulcers were due to "synergistic action" or to any infection at all. There was no evidence of malnutrition, blood dyscrasia or a general vascular process such as periarteritis nodosa or the Sanarelli-Shwartzman phenomenon. It is suggested that the ulceration was due to an excessive tissue reaction to some undefined injurious agent, and the term "allergy" should be expressly avoided. Development of psychotic illness in both patients under treatment was regarded as pure coincidence.

► [In view of the increasing number of reports about hypo- and agammaglobulinemia associated with chronic and progressive ulceration of the skin, every such case which fails to respond to conventional forms of therapy should be investigated concerning any possible abnormalities in the gamma globulin fraction of the blood proteins. The striking response to ACTH or cortisone would not speak against a gamma globulin deficiency, as such hormonal treatment has been shown to be effective in several cases of ulcerations based on agammaglobulinemia.—Ed.]

Pyoderma Gangrenosum: Report of Case Controlled by Cortisone. Chronic, undermining, burrowing ulcers which spread peripherally and are characteristically resistant to treatment have been described under such titles as pyoderma

(9) T. St. John's Hosp., pp. 31-34, Autumn, 1953.

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[1] A.M.A. Arch Dermat. 74: 543-544, November 1956

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buffalo hump more rapidly and more often than patients receiving equivalent therapeutic doses of hydrocortisone.—Eds.]

Hydrocortisone Ointment Bases Clinical Evaluation of Effect of 11 Different Vehicles Containing 1% Hydrocortisone is presented by Frederick Kalz and Allene Scott (Royal Victoria Hosp Montreal) Evaluation was made of oily water-repellent bases, hydrophilic absorption bases water in-oil and oil-in-water emulsions and oil free bases. In assessment of final results, the type stage and location of the dermatosis were important. Emulsions with an outer oily phase were considered greasy those with an outer aqueous phase gave a feeling of dryness. In the 264 patients, aged 6 months to 72 years, diagnoses included atopic dermatitis, seborrheic dermatitis, pruritus perinei and contact dermatitis

Bases representing the two extremes the greasiest and the dryest gave poorest performance. Short term application did not show the marked differences of long term use. In seborrheic dermatitis, the reaction to the bases appeared improved by addition of water so that the drying ones were better No distinctive features were noted in contact dermatitis d it governed the choice of bases The 138 patients with atopic dermatitis themselves quickly determined which bases were best for them they had an all or nothing reaction Five vehicles proved to be most generally useful—an oily absorption base, two water in-oil emulsions and two o l water emulsions As rule the thinner the skin the more suitable the greasy bases. Folds where there is increased perspiration, such as the groin axillae and antecubital fossae did best with drier bases. The patient with atopic dermatitis was most difficult to satisfy subject v ly patient with contact dermatitis accepted almost all bases without trouble Estimate of the degree of dryness made by the patients corresponded closely with the known water content and properties of a base

Differences of therapeutic action of hydrocortisone in different vehicles not determined by the influence of the base on the penetration of the hormone, but by compatibility of the base with the disease and its locations No all purpose best base can be devised, and individual choice of base with consideration of type and location of the skin disorder is prerequisite for optimal therapeutic results

(M A Arch Dermat 3 355 360, April, 1954.

esting to see what large doses given intramuscularly would have achieved in this case. While it is difficult to fully evaluate the lowered gamma globulin blood level it may have resulted from the cortisone therapy Theoretically one might assume that suppression of production of gamma globulin, which contains many antibodies, might make the lesions worse. Apparently however the other effects of systemic cortisone therapy sufficiently outweigh this particular action to produce clinical improvement.—Eds.]

Prednisolone Topically and Systemically Clinical Evaluation in Selected Dermatoses (Preliminary Report) part of a project to determine the effects of various corticosteroids on skin electrolytes is presented by Lawrence Frank and Conrad Stritzler[2] (State Univ of New York, New York City) who administered 0.25% and 0.5% prednisolone topically in petrolatum and liquid petrolatum and 1% hydrocortisone in a similar base to contralateral areas of 256 patients. Prednisolone was given orally to 67 patients with various dermatoses The initial dose of 40 mg daily was gradually reduced to a maintenance dose of 15-25 mg/day No dietary or sodium restrictions were imposed.

Topically the prednisolone was less effective than the hydrocortisone ointment Among 256 patients prednisolone ointment irritated the inflamed skin of 9 The response to hydrocortisone was generally quicker and more apparent and relief from pruritus was outstanding Systemically prednisolone produced by dehydrogenation at the 1 and 2 positions of the hydrocortisone nucleus was an active and potent corticosteroid Its spectrum of responsive dermatoses was similar to that of hydrocortisone, but it was four times as effective by weight In therapeutic doses it produced no sodium and fluid retention potassium depletion or hypertension Side effects were increased appetite abdominal pain moon face and severe depression but only in a few patients. No hypertension sudden weight gain edema or glycosuria occurred in this series.

► [Like the authors our own experience with the topical use of prednisone and prednisolone ointments in 0.5% concentration showed them in most cases to be about equally effective but in some somewhat less so than hydrocortisone 1% ointment.

In studies together with Frolow and Sulzberger, the junior editor encountered some eruptions that became worse following the therapeutic use of early batches of experimental prednisone and prednisolone ointment with later batches this undesirable effect was not noted.

In our experience, patients receiving these compound systemically showed moon facies, supraclavicular and suprasternal notch fat pad and

(2) A.M.A. Arch. Dermat. 72 547-549 December 1955.

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[3] A. M. A. Arch. Dermat. 7 333-368, April, 1954.

Effect of Cortisone in Alopecia Areata and its mechanism of action were studied by Hugo R. Rony and David M. Cohen[4] (Chicago Med School) to clarify whether the hormone has direct peripheral action on the hair organ (*a*) an indirect action i.e. by a substance into which cortisone may be transformed (*b*) or an action by substances which cortisone may produce through some of its many actions on other glands or metabolic processes (*c*) Observations to the effect that cortisone topically applied in the form of ointment or spray did not produce topical hair growth in alopecia areata would tend to indicate that mechanism (*b*) or (*c*) may be wholly or partly operative However the following experiment clearly establishes the sole validity of mechanism (*a*)

Man, 54 following a stress situation, developed alopecia universalis. He received 150 mg cortisone orally/day for 2 days, followed by 125 mg daily for 35 days. This therapy was discontinued because of a severe acneform eruption of the face, which disappeared in three weeks. No hair growth was observed over a year Injections of hydrocortisone acetate, 50 mg./cc. in doses of 0 05-0.10 cc. were given twice weekly into an area the size of a dime on the extensor surface of the right lower arm. Four weeks later hairs emerged from the injected area only No further injections were made. The hair continued to grow for six weeks, reaching 5-10 mm. in length. The hairs, white at first became pigmented later Injections into a small area of the scalp brought similar results. A control area on the left forearm was treated with 0.2% fluorocortisone acetate ointment and another area with injections of testosterone propionate. No hair growth was observed in either area.

Hydrocortisone injected intradermally can induce hair growth in injected areas and may be useful where small areas of the scalp are involved. This indicates that hair growth following the oral administration of cortisone in alopecia areata must *also be attributed to a direct action of cortisone on some* structure in the corium. Hydrocortisone ointments fail to accomplish this because apparently not enough hormone is absorbed into the skin to be effective

► [That local injections of hydrocortisone acetate, prednisone and prednisolone can stimulate local hair growth in areas of alopecia areata and alopecia universalis has now been confirmed by many investigators The mechanism of this action, however is as yet unknown. The evidence is not yet sufficient to credit hydrocortisone or the other compounds with a direct action on the hair producing organ.—Eds.]

Treatment of Keloids with Topical Injections of Hydrocortisone Acetate is reported by G Asboe Hansen H Brod

(4) J Invest. Dermat. 25:285-287 November 1955.

thagen and Lis Zachariae[3] (Copenhagen) Of 56 keloids observed, 28 arose from vaccinations, 4 from acne and 24 from burns, operations or contusions. Injections of hydrocortisone acetate (25 mg./mL) in total doses of 35-725 mg were limited for each injection by size and consistency of the keloids, which had existed for an average of 33 months. Injections were given at intervals of 8-20 days

Of the keloids treated 51 were softened and flattened 41 to the urrounding skin level 32 disappeared entirely and 5 howed no change. Only 1 of 35 patients followed showed recurrenc after six months. In some cases a flaccid, wrinkled unsightly atrophic flap of skin without fibrous content was l ft In 10 instances atrophy was produced beneath and adjacent to the njected areas.

Mi croscopically the intense metachromasia with toluid ne bl e normally seen n fresh keloids was fainter or absent and number of mast cells reduced. At the end of 7 12 days, highly metachromatic granulated mast cells and ground substance i creased. The picture gradually shifted to that of normal keloid Optimal time for repeat injections is probably 7 12 days part.

The therapeutic effect of hydrocortisone on keloids is probably on the ground substance between fibrils which normally adherent in bundles are now afforded a chance of moving n relation to each other Fresh keloids respond more rapidly than ld. Cosmetic results are generally good, but transitory soft tis atrophies may occur

► [These very favorable results are confirmed by a much smaller series of keloids similarly treated with injections of hydrocortisone by Eliassow and Rosenfeld at the Skin and Cancer Unit. However these investigators noted a sloughlike crust following the hydrocortisone injections which preceded the flattening of the keloids Probably anyone who has done much intracutaneous injecting of hydrocortisone acetate solution is familiar ith the mild atrophy of the area which may follow The possibility of such an occurrence should be taken into consideration when contemplating intracutaneous hydrocortisone injections.—Eds.]

B Physical Therapy

Verrucae Vulgares et Plantares Treated with Ultrasoft X-rays. Erik Andr Knudsen and E. Amdrup[4] (Kolding Denma k) used the techn of Ebbehøj in treatment of

3 A M Arch Dermat 7 142 143, February 1956
Acta dermat.-venereol. 35 [illegible] 955

warts in a manner that is unlikely to cause radiation sequelae

METHOD.—The callosity over a plantar wart is removed by a sharp spoon or knife None of the surface is removed in verruca vulgari Lead foil 0.3 mm. thick is used for shielding In verruca plantaris a hole is cut the size of the wart plus several millimeters of callus tissue. In verruca vulgaris, the aperture corresponds exactly to the size of the wart to avoid irradiating adjacent tissue. The lead shield is fixed to the skin with tape. A dose of 3 000-4,000 r is administered in one treatment to the area in about one minute. Since 1945 a Machlett tube with a beryllium window has been used. Factors are target skin distance 10 cm., 30 kv 20 ma. and 0.2 mm Al as an extra filter for which the half value layer is equal to 1 43 mm. of skin. A ray of dangerous quality is believed to have a half value layer of about 3 mm. of skin, at which level vascular and cicatricial effects might be produced. The warts become tender in two to three weeks and dry and fall off in four to five weeks. If the result is unsatisfactory treatment is repeated after six weeks.

Of 500 patients treated in 1952 475 replied to a follow up questionnaire in 1954 Of this group 422 (88.8%) were cured. Altogether they had 1,043 warts of which 951 (91.2%) disappeared. Of 668 verrucae vulgares (253 patients) 599 (89 7%) disappeared (218 patients cured) Of 375 verrucae plantares (222 patients) 352 (93 9%) disappeared (204 patients cured) Treatment was given twice to 69 verrucae vulgares and 33 verrucae plantares Twenty six warts (23 verrucae vulgares and 3 verrucae plantares) in 16 patients recurred on the previous site The treatment seems as effective as with harder rays and is less dangerous

► [These therapeutic results are unusually satisfactory if one judges by the percentage of cases reported. If these results are achieved without serious sequelae later on, this form of therapy may well become a method of choice in the management of most warts.—Eds.]

Ultrasoft Roentgen Rays in Treatment of Hemangiomas Follow up Examination of 400 Cases of Strawberry Marks and Port Wine Stains. From 1940 to 1952 E Amdrup and G Knudsen[7] (Kolding Denmark) treated 315 elevated and 87 flat hemangiomas with x rays First a Siemen tube was used giving a beam with a half value layer of 2 02 mm of skin at 30 kv and of 1 15 mm of skin at 20 kv Most elevated hemangiomas were treated at 30 kv whereas the thinnest strawberry marks and flat hemangiomas received the softer radiation A Machlett tube with a beryllium window and a focus skin distance of 10 cm was later used A few hemangi

(7) Radiology 64 823-834 June 1954.

omas were treated with Bucky rays, usually in fractionated dosage, with 500 r at each session. Except in these few cases a large single dose was given. At present, the authors invariably use a single dose of 800-1,200 r. The adjacent unaffected skin is protected by a thin shield of lead foil 0.1-0.3 mm thick which is sufficient to stop the ultrasoft rays. A hole corresponding to the form and size of the hemangioma is cut in the lead foil. Elevated hemangiomas must be compressed during exposure; otherwise the great amount of blood in these lesions absorbs much of the ultrasoft rays, resulting in an undue difference in the dose delivered to the surface and to the deeper portions.

Small hemangiomas rarely required more than one treatment; medium and large lesions often needed two or occasionally three. More than three exposures of 800-1,200 r were never given.

After treatment, some hemangiomas disappeared without a scar; others left a more or less pronounced scar. Scarring was sometimes attributable to pretherapeutic ulceration and infection of the hemangiomas. Best cosmetic results were achieved with small hemangiomas.

Of 315 strawberry marks, 212 (67.7%) completely disappeared with no or only a slight scar. All the less satisfactory results were obtained after treatment with rays having a half value layer of at least 2 mm of skin.

Small port wine stains most frequently disappeared, leaving only a slight scar or none after one or at most two treatments given four months or more apart with this technic. Large hemangiomas became less conspicuous. There was no scarring in the irradiated area after a single dose of 1,000-1,200 r. After two administrations of this dose slight atrophy usually developed, and three exposures resulted in a slightly more distinct scar.

► [The results obtained in this series treated with -radiation of 20-30 kv are worthy of attention. The high percentage of favorable responses without radiation sequelae (considering, of course, the follow-up period of 2-12 years) favors the principle of using low kilovoltage radiation. Furthermore, the authors often waited many months between treatments, thus affording the opportunity to observe the effects of a single treatment.

We heartily endorse this approach as the chances of producing radiation sequelae and, in particular, any alterations in bony development, are minimal. The routine of irradiating and waiting is in keeping with the principle used by the late Dr. George M. MacKee, the administration to hemangiomas of relatively small doses of radiation (radium) with the thought

that the natural course of involution would be hastened and that additional doses might not be necessary

It is becoming increasingly evident that many dermatologic disorders may be satisfactorily managed with x-radiation of lower kilovoltage than has been customarily used in the United States. We hope that this trend will continue and that the future will bring additional investigations in this direction.—Eds.]

Soft Radiation Tube with Voltage Ranging from 10 to 100 Kv Are Soft Radiations Up to 100 Kv Necessary for Adequate X ray Therapy? The beryllium window of modern superficial x ray therapy tubes not only permits grenz rays and similar soft radiations to pass through but is also stable and resistant even to 1 000 kv Due to these two properties of the beryllium window universal x ray sets could be built with one tube, the therapeutic range of which could extend from grenz rays to deep x radiation. Such an apparatus, with a range of 10-100 kv is described by Carl Georg Schirren[8] (Univ of Munich) By use of a special tube with an external anode, body cavities can be treated For simultaneous use of *both tubes four switch steps are provided when one tube* only is employed all eight switch steps can be used Target skin distance is 8 15 and 30 cm The set is equipped with a fully automatic filter safety device, permitting high voltage to be switched on only when the filter corresponding to the required switch step is inserted Wrong filters are indicated by a visual device

Enormous dosage effects of unfiltered 100 kv irradiation are due to the excessive portion of supersoft rays This instrument which in an emergency can also be used for generation of irradiation of tissue half value depth of 50 mm (100 kv 0 4 mm Cu) i e. deep therapy does not offer any real advantage in comparison with other soft radiation sets of 10-50 kv The latter are less expensive, require fewer safety installations and in most cases are sufficient for the dermatologist as most dermatoses do not extend deeper than 3 mm

► [Ever since the introduction of the so-called combination dermatologic x-ray units which take advantage of the versatility of beryllium tube windows, the editors have stressed *the potential* dangers of such equipment. Once again we caution against the use of such units *unless automatic devices make it impossible* to deliver radiation above the grenz ray range without the necessary filters having been inserted. Visual devices indicating failure to insert filters do not fulfil these requirements.—Eds.]

Acute Radiodermatitis after Use of Modern Superficial Therapy Apparatus with Beryllium Window G Bonse[9]

(8) Hautarzt 7 32 34, January 1956.
(9) Ibid pp. 76-78, February 1956.

(Uni of Wurzburg) reports a case of third degree radiodermatitis caused by carelessness of the radiotherapist and failure of the automatic filter safeguard.

A doctor with psoriasis vulgaris, received on the dorsum of the left hand 2,400 r (29 kv unfiltered, 20 cm. target skin distance) in one single session. On hospitalization 16 days later he had a sharply outlined, extremely edematous, nearly jelly-like, dark red to brownish, painful erythema with blister formation involving the dorsum of the left hand and dorsal surface of the basal phalanx of each finger and of both phalanges of the thumb of the left hand. High doses of cortisone, beginning with 200 mg daily and decreasing to a total of 4,850 mg, 7 Gm. tetracycline orally combined with high doses of vitamin E, and 6,800,000 units of penicillin (parenterally) were given. After the left forearm was placed in a plaster of paris cast (with the dorsal surface uncovered), hydrocortisone ointment and *tyrothricin eucerin* were applied to the dorsal surface of the hand. Rapid involution of signs and symptoms followed, but three weeks after irradiation skin temperatures taken on corresponding areas of the hands showed differences of 0.5-1.2 degrees C. Intense pain ceased six to eight hours after treatment was started. When he was discharged seven weeks after irradiation, there was pronounced atrophy of the skin, with loss of hair on the dorsum of the left hand; the skin was not sclerotic, but recurrent psoriatic lesions were present.

Whether cortisone, which brought about the good results, may also prevent late sequelae cannot now be stated.

► [In past editorials and in the leading article of the 1955-56 YEAR BOOK, the editors have repeatedly stated that they are opposed to the use of combination x-ray and grenz ray machines, unless there are absolutely *foolproof safety* devices which could be depended on to prevent accidents such as this. Undoubtedly similar accidents are occurring but are not being reported.

Radiation procedures require the fullest attention of the operator in order to avoid possible errors. For example, in our practices, we have made it a habit that whenever filtered radiation is used somebody besides the operator himself checks the x-ray machine settings and makes certain that the proper filter is in place.—Eds.]

Malignant Melanoma. Bertel Jørgsholm and Inger Engdahl (Copenhagen) report an analysis of a series of 141 female and 78 male patients, some treated by surgery, some by *radiotherapy and some by a combination of both.* The total five year cure rate was 28.8%. Surprisingly good results were obtained from radiotherapy alone. After five years, 9 of 15 patients treated by irradiation alone and 2 given irradiation for local recurrences after surgery were symptom free.

Man, 75, with chronic post traumatic ulcer on the left lower leg of 10 years duration noticed darkening and nodularity of the local skin shortly before he was seen in 1947. Examination revealed an

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Acta radiol. 44: 7-433, November, 1955

that the natural course of involution would be hastened and that additional doses might not be necessary

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(8) Hautarzt 7.32-34, January 1956

(9) Ibid., pp. 76-78, February 1956.

to a density of 265 μc of P^{32}/sq cm. Average dosage rate in this energy range at a depth of 0.8 mm is only 50% of that at the surface, which restricts use of these plaques to lesions not thicker than 1 mm. without giving a necrotizing dose to the surface layers. Lesions over bone are relatively safely treated. Lead shields should be used over eyes. Damage to the hemopoietic system is negligible. Local applications of metallic salts should be removed in advance because they will absorb much of the beta radiation. The plaques are fitted over the lesion and strapped on for the prescribed time. Their flexibility is a particular advantage for this type of lesion

In 17 patients treated with the technic results were excellent, although long observation for skin atrophy is needed. Doses of 450 r were given for these lesions two three or four times on areas as large as 100 sq cm producing adequate fading without severe local reactions. Erythema usually started on the 7th day and had faded by the 28th. Four nevi disappeared entirely 11 were definitely paler and still paling and in 2, results were unavailable

It is concluded that this technic is useful in treatment of superficial vascular nevi including capillary nevi plaques are easy to handle because they can be shaped to fit cavities or protuberances The technic provides a safety factor for underlying structures since penetration is not as deep as with a radium plaque

► [Here is another example of selecting the type and form of radiation based on the size and depth of the lesion to be treated. This principle of not overshooting the mark is one that is becoming more and more recognized in dermatologic radiation therapy Judging from the photographs in the article, capillary nevus as used by the authors refers to the deeper red and purple nevus flammeus or port-wine mark, as well as to sharply defined lesions, elevated slightly above the surface of the surrounding normal skin and with an irregular surface According to the data given by the authors, the beta radiation from P^{32} has its greatest effect within the first millimeter of tissue which corresponds to the approximate thickness of the lesion being treated —Eds.]

X-ray Exposure in Dermatology Personnel, as recorded for 3½ years by photographic film dosimetry reported by C Thomas Jansen and Arthur C Curtis[a] (Univ of Michigan) The energy range of operation was 94-100 kv A Du Pont type 552 film packet was used in all recordings, mounted in a Tochol n metal monitoring badge with an open window and a filter system incorporating 1 mm. aluminum, 0 375 mm

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[a] A.M.A. Arch Dermat [illegible], January 1954

elevated, bluish red to black melanoma, 4×2 cm., on the leg. There were no palpable lymph nodes. Biopsy disclosed malignant melanoma.

Because of his advanced age, x-ray therapy using two tangential fields was given on an outpatient basis. This caused edema and slight regression. He was hospitalized and treated with heavy fractionated roentgen contact therapy using two small central fields and eight small marginal fields around the elevated part of the tumor. A total of 2,400 r was delivered to the two tangential fields in 9 days and, after an interval of 3 weeks, 6,500 r was delivered to the central part in 19 days as well as 4,250-5,600 r to each of the marginal fields in 19-25 days. The tumor became flattened and showed marked exudative reaction, replaced by necrosis that healed slowly in nine months. The lesion remained healed and in April 1954 (seven years after treatment) there was only slight dry crusting and atrophy of the irradiated skin area with flat, residual pigmentation in the center and no evidence of edema or symptoms.

Postpuberal patients in whom a diagnosis has been made with as much certainty as possible without biopsy should be treated with wide excision or electrocautery with a 3-4 cm. margin of healthy tissue including fascia. Plastic repair can follow. Lymph node dissection is indicated for evidence of metastases. Major amputations should be reserved for otherwise inoperable cases (extensive cutaneous spread or multiple regional nodal involvement). In elderly or debilitated patients adequate radiotherapy offers possibilities that must not be neglected.

► [Another contribution which supports the opinion and findings of other European investigators that x radiation apparently can be used successfully in the management of some selected cases of malignant melanoma. The present series includes some patients who were cured by maid e radiation therapy alone, without subsequent surgery. (See also the 1955-56 YEAR BOOK, p. 273.—Eds.]

Radiophosphorus in Treatment of Capillary Nevi is described by D. S. Anderson Roe, Christine Hodges, G. S. Innes and L. I. Pope[2] (London). Investigation was limited to the deeper red and purple marks. Radioactive phosphorus P^{32} emits pure beta rays with a maximal energy of 1.7 Mev and a mean effective energy of 400 kv.

METHOD.—A piece of blotting paper shaped to the lesion is ruled in 0.5 cm. squares. A drop of P^{32} solution is placed on each square, the paper is dried in an oven at 90 F. and when dry is reloaded from the other side. It is mounted on a lead sheet, 0.22 mm. thick, covered with Alkathene sheets and with a lead window the size of the active area. Edges are sealed with Cellotape.

These plaques give 1,000 r/hour at the surface if loaded

(2) Lancet 2 1111-1113, Nov. 26, 1955

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A M A Arch Dermat 73 44-48, January 1956

cadmium and 0.675 mm lead. Most recent reports express permissible weekly doses as 300 milliroentgens (mr) in blood forming organs gonads and eyes and 600 mr in the basal layer of the epidermis This report includes 462 film badges each covering a two week period of exposure. The recording technic permits minimal readings of 30 mr per two week exposure period Even when x ray therapy was administered daily the exposures were well below accepted permissible levels except in one instance (0.21%) in which an exposure above 600 mr was recorded for a two week period and in which a lax attitude toward exposure possibilities was admitted by a nurse technician In the dermatologic staff using x ray therapy daily the dose noted was well below the accepted permissible dosage of 300 mr per week when reasonable care for self protection was exercised.

► [It is generally taken for granted that operators of dermatologic x ray equipment are safe from radiation exposure while administering treatments. This is undoubtedly so where modern shielded shock-proof units are being used and the operator is properly protected behind leaded partitions. To be absolutely certain that one is not operating under a false feeling of security film dosimeter badges or some similar measuring devices should be used to measure the actual amount of radiation reaching the person. In 1949, the junior editor used film badges in private practice for three months. Badges were placed behind the operator's protection screen or were worn by the operators for a one-week period, at which time they were changed. At no time during the three-month study did a film badge register any radiation whatsoever.—Eds.]

Liquid Nitrogen in Dermatology is discussed by B Duperrat and Cauvin[4] (Paris) Liquid nitrogen is an odorless and colorless fuming liquid used in dermatology since 1950 because of its thermic effects after short application to the skin (Allington) In contradistinction to liquid air handling liquid nitrogen is safe it causes neither chemical changes nor burns

TECHNIC.—Liquid nitrogen is poured into small metal containers and applied with 12 15 cm. long wooden applicators, one end of which is wrapped with cotton wool (for small warts no cotton wool is used) Since liquid nitrogen evaporates rapidly fast application and grouping of patients are essential. For 40 patients, about 1 L. of liquid nitrogen is needed. Duration of applications varies small warts require 2 3 seconds without pressure, large warts up to 30-60 seconds with pressure. Verrucae of the palm located on pressure points, with the appearance of plantar warts and often painful are better pared down on the day preceding treatment. Application of liquid nitrogen is followed by pricking or burning pains, minimal

(4) Ann. dermat. et syph. 82:626-634 Nov Dec 1953

in parts of the lateral aspects of fingers and on the dorsum of hands, more marked on periungual, subungual and palmar warts. However pain is not unbearable, provided surrounding normal tissues are spared as much as possible. Burning and stinging sensations are followed by slight itching and tingling when revascularization starts, but do not last more than 12-24 hours. After three or four days, treated lesions dry and turn brownish or form a serous, sometimes hemorrhagic blister with subsequent crust formation. After about 10-15 days, healing is complete, showing a fine, flat, pinkish scar occasionally a pigmented halo.

Treatment with liquid nitrogen was done in about 400 cases of verrucae vulgares neither disfiguring scars nor keloids were observed. Recurrences were seen in three patients only where warts were subungual or situated in finger folds. In two or three patients warts did not respond to treatment these were plantar warts and palmar warts on pressure points with marked surrounding callus formation. In addition infectious papilloma (three cases) venereal warts (one case) senile keratoses and seborrheic warts (three cases) one case of hypertrophic scar (which was treated at 10 sessions) two cases of neurodermatitis of the neck and one case of disseminated lichen corneus of the leg were treated successfully. In one patient with neurodermatitis of the leg, results were less satisfactory. It is planned to try this treatment also in angiomas, plaques of lichen corneus and hyperkeratotic eczemas.

► [Once again the original observations of Allington (1950 YEAR BOOK, p 142, and California Med 72 153, 1950) are confirmed. If liquid nitrogen is as easy to obtain as solid carbon dioxide, in all probability it would be used much more frequently and in a greater number of dermatoses. While solid CO_2 is not as cold as liquid nitrogen, it still may be used satisfactorily in the treatment of some of the same conditions. Verrucae vulgares, for example, require firm pressure for 15-20 seconds, depending on the size—the larger the lesion the more firm the pressure and the longer the exposure.—Eds.]

C. Other Therapy

Dark Room Treatment in Dermatitis Medicamentosa of Exposed Parts. Edwin Sidi and Marc Hincky[5] (Paris) found that photosensitization plays an important role in dermatitis medicamentosa caused by topical sulfonamide therapy or following local application of antihistamine cream. After prolonged or combined internal and topical administration of these drugs and within a few hours after light exposure an

[5] Presse méd. 63 1843 1845, Dec. 21, 1955.

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in warts of the lateral aspects of fingers and on the dorsum of hands, more marked on periungual, subungual and palmar warts. However pain is not unbearable, provided surrounding normal tissues are spared as much as possible. Burning and stinging sensations are followed by slight itching and tingling when revascularization starts, but do not last more than 12 24 hours. After three or four days, treated lesions dry and turn brownish or form a serous, sometimes hemorrhagic blister with subsequent crust formation. After about 10-15 days, healing is complete, showing a fine flat, pinkish scar occasionally pigmented halo.

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► [Once again the original observations of Allington (1950 YEAR BOOK, p 142, and California Med 72 153, 1950) are confirmed. If liquid nitrogen is as easy to obtain as solid carbon dioxide, in all probability it would be used much more frequently and in greater number of dermatoses. While solid CO_2 is not as cold as liquid nitrogen, it still may be used satisfactorily in the treatment of some of the same conditions Verrucae vulgares, for example, require firm pressure for 15-20 seconds, depending on the size—the larger the lesion the more firm the pressure and the longer the exposure.—Eds]

C. OTHER THERAPY

Dark Room Treatment in Dermatitis Medicamentosa of Exposed Parts. Edwin Sidi and Marc Hincky[3] (Paris) found that phot sens tization plays an important role in dermatitis medicamentosa caused by topical sulfonamide therapy or following local application of ant histamine creams. After prolonged or comb ned internal and topical administration of th drugs nd within few hours after light exposure an

(3) Presse méd. 63 1843 1845, Dec 1 1955

extensive dermatitis of the uncovered parts of the body (face neck and forearms) *develops accompanied by redness* edema, oozing of the areas involved puffy eyelids, lacrimation photophobia and occasionally rise in temperature Often there is a marked contrast between an acute dermatitis of the exposed parts and a comparatively mild dermatitis of the areas protected from sunlight by clothes, bracelets, wristwatches etc Later the acute dermatitis changes into a chronic condition showing dark red fissured squamous, parakeratotic, thickened lichenified areas and finally pigmentation and slight atrophy suggesting pellagra rather than eczema. Conjunctivitis and ectropion of the eyelids may be present The clinical appearance may resemble lupus erythematosus which however responds less frequently to antimalarial treatment than do other cases of lupus erythematosus

Photo ensitizing drugs include coal tar derivatives *of fluorescein* (eosin) and acridine (gonacrine) sulfonamides the paraphenylenediamine group (including local anesthetics like procaine) and thiazine derivatives (multergan and chlorpromazine)

In dermatitis medicamentosa the patient should avoid exposure to sunlight for which purpose the dark room proved effective At the onset of acute photosensitization complete healing may occur within one week and in chronic cases, within 10-15 days of dark room confinement with no treatment other than wet dressings Results are usually satisfactory but relapses sometimes occur after exposure to sunlight for which a protective sun cream should be used particularly from February to April Vitamins PP E and B complex and antimalarial agents including nivaquine have been given internally *but the response has been unreliable*

► [This work goes to show that to keep a person "in the dark is not always detrimental! The observation that complete avoidance of exposure to daylight is effective in helping to clear these cases of photodermatitis is of great potential practical importance. The months of February to April are considered the most *risky by the authors, apparently because in cases* of persistent light sensitivity some (specifically and/or nonspecifically) acquired tolerance to light is lost during the w nt A recurrence is then most likely during the sunny spring months.—Eds.]

Effect of Nonmedicamentous Enclosure and "Dermatologic Rest" on Eczema, a technic of "hospitalizing part of the diseased skin with plaster splints is described by R D

G Ph. Simons[a] (Amsterdam) Patients were selected whose eczema had not been cured by usual methods and who had not had x ray therapy for at least six months. Surgical rest, complete immobilization is distinguished from dermatologic rest, in which the skin is protected against external stimuli such as scratching renewing ointment or cleansing but with only moderate restriction of movement. Enclosure entirely in plaster was more satisfactory than in plaster and bandage Treatment lasted two to four weeks. After plaster removal the skin beneath was notably scaly which was considered normal insensible scaling rather than eczema. Moist eczema is a contraindication for plaster bandaging Most of the 90 adults investigated had chronic lichenified and/or itchy eczema of face, hands, arms or legs. All the 13 children had atopic eczema.

Cure or great improvement was obtained in 53 patients (7 children) no effect was seen in 31 adults eczema became worse in 19 adults and relapse occurred in 23 after two to six weeks. Failures were more frequent in patients treated for only two weeks and in those with herpetoid or weeping eczema

The following conclusions are drawn from the study Dermatologic rest by enclosure is of striking effect in most cases and failures are no more frequent than with other therapy This modality may have the same beneficial psychic action as hospitalization and like the latter would also free the patient from allergen contacts at home The untreated skin usually shows no reaction although in three cases a beneficial symmetrical co-reaction was observed after application of the plaster bandage Although plaster enclosure does not prevent relapse, it acts more quickly than most other methods Ointment bandages are more effective than ointment alone probably through physical protection rather than chemical action Effect of the plaster bandage is probably not primarily psychic since black salves radiation and poorly fitting bandages were less effective. The proposed purpose of this investigation has been to show that enclosure alone can have a favorable effect on eczema.

► [Of a total of 103 patients (adults and children) 53 were benefited, and of these only 30 remained free from lesions for more than two to six weeks. Perhaps this represents a good enough result for a group of cases

[a] J Invest Dermat 25 363 374, December 1955

which had previously failed to respond to "usual methods" of therapy *Therefore, this form of therapy deserves further trial in carefully selected cases.* The main interest of the procedure, however appears to be in the mechanism which produces these results rather than in its value as a form of therapy —Eds.]

"Co-reaction" of Untreated Areas in Psoriasis was studied by H W Siemens[7] (Univ of Leiden) in a further series of patients It was reported previously that in some dermatoses, particularly in psoriasis spontaneous healing may occur furthermore, that with the aid of the therapeutic window considerable improvement even complete healing may be demonstrated in *psoriatic patches not included* in topical antipsoriatic treatment. In the present and previous series of 38 patients with psoriasis spontaneous healing occurred in 13 Healing was total or regional some areas, e.g the arms, did not clear or others e.g., elbows and knees improved *only slightly* The other *24* patients revealed "co-reaction Of the 11 patients in the present series 9 showed complete and 2 incomplete "co-reaction It is therefore concluded that co-reaction occurs rather regularly in patients with psoriasis and is absent only rarely In two patients small rather recent lesions which appeared in the preobservation period "co-reacted" more slowly or not at all In two patients, both of whom were hospitalized on two occasions, the same set of tests were carried out during both hospitalizations with identical clearing of the psoriasis lesions in the therapeutic window on both occasions

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(7) Arch. klin u. exper Dermat. 202 247 253, 1956.
(8) Brit. M. J 654 657 Mar 24, 1956.

confirmed by the closed patch technic and occasionally subcutaneous testing is used, but with caution

Five case histories are recorded which show that a minute tolerated subcutaneous dose of either penicillin or streptomycin can suppress specific allergic reaction to skin contact with an antibiotic for a short time, that maintained daily treatment with such doses suppresses continuously a reaction to handling an antibiotic and that a relati ely lasting spon taneous tolerance of handling contacts may be developed after prolonged cover treatment. In a sixth case the same suppressive effect has been used to co er isolated occa ions f handl ng

Basically a minute subcutaneous dose of penicillin or streptomycin can specifically prevent local and remote reac tion to handling the same agent for a short time Doses of 1 20 units are ffective for 8-24 hours. Spontaneous fluctua tion of sensitivity is common, and complete "hardening may occur where reaction is mild enough to permit con tin ed contact, but severe reaction always leads to an increased sensitivity One unit of either antibiotic is a safe dose for a patient not in acute reaction and with no hi tory of severe generalization. Treatment can reasonably be at tempted at 1 2 units/day in mild cases and 5-10 units/day in more severe cases Local reaction at the injection s te may appea as a delayed erythema with varying degrees of superficial infiltration

The co er treatment appears free from haza d unless in jection are gi en at ll chosen times, in contrast to th exceedingly arable response to treatment with rising doses. With cover treatment, the patient is usually able to handle the antibiotic without reaction sooner than with the rising dose treatment. Classic desensitization with rising doses is uccessful as a seasonal prophylaxi for hay fever but when applied t a skin-contact allergy t has serious limitations. If however a cover treatment permits handling of the anti biotic without reaction, the conditions for the occurrence of natural harden ng are more simply satisfied than by work g up t high dose.

► [A remarkable report, the contents of which are most interesting from both practical and theoretical viewpoints. This technic deserves further trial I cases in which there is clinically suggestiv evidence of reduced cutaneous sensitivity accurate quantitative drop or patch tests with dilu-

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(8) Brit. M. J 454-457 Mar 24 1956.

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(7) Arch. klin. u. exper. Dermat. 202: 247-253, 1956.
(8) Brit. M. J. 1: 654-657, Mar. 24, 1956.

twice daily the dose was increased over 8-12 weeks until 0.5 Gm. twice or three times a day was tolerated. After a final test dose of 1 Gm. three times a day a patch test was repeated in 10 days. This was successful in three patients.

F e subjects highly sensitive to streptomycin responded best to desensitization by graded intramuscular injections starting w th small doses of the order of 10 µg.

► [The clinical evidence of loss of sensitivity after specific hyposensitization in some of the subjects together with the negative patch test reactions should encourage much more extensive efforts in this important segment of practical immunology.—Eds.]

Aqua Ivy: Toxicity Studies on Guinea Pig and Treatment of Sensitive Cases. Richard E. Passenger, Will Cook Spain a d Margaret B. Strauss[1] (New York Univ. Bellevue Med. Center) fou d that guinea pigs who received the full human dose f aqua ivy subcutaneously were not made more skin sensitive to poison y as demonstrated by contact test with quantitat e serial dilutions. Nephritis, even with large doses of aqua ry was not found on autopsy in guinea pigs.

The authors admin stered 121 prophylactic series of aqua ry jections to human patients. Each had existing dermatitis typical of the eruptio caused by poison i y or oak or began treatment because of a history of one or more years of difficulty recurring annually. An excellent result was one n which th rest of the year elapsed with appearance of less than three or four 12 mm. macules or papules. Larger areas f macules and papules regarded s inconsequential by the patient was considered a good result unles the area wa greater than about 3 sq in. Palm-sized or larger areas any esiculation or fa lure of the injection to help in the patient s opin ion was poor esult. Based on these ough criteria 63 courses (5 %) ga e xcellent prophylact c results, 50 (41%) good esult and 8 (7%) poor results.

A series f one to fou njections wa gi en for v dermatit present at the initial visit to 85 patients. Acut esiculation oozing of relati ely large area from ntimate e posure to or cases where ther were se eral full doses of i y n oil d ri g the preced g 10 days neces itated w thholding jection. A erage phylactic treatment for adults w th mild t moderat cases f dermat tis enenata consisted f subcutaneous njections every two to four day of 0.1 0.2 and 0.3

tions of penicillin and streptomycin should prove of much help in establishing the degree of lessening of sensitivity which occurs under such "cover" treatment.—Eds.]

Treatment of Contact Sensitivity to Antibiotics and Related Substances in Nurses is discussed by Stanley R. Wood[9] (Birmingham England) Treatment by desensitization is indicated when sensitivity is high and contact likely to continue If the antibiotic is absorbed by mouth the oral method is advantageous Treatment assumes that antigen and antibody and products of their interaction follow the law of mass action



$$A + B \rightleftharpoons C + D$$

(antigen) (antibody) (products slowly excreted)

In the sensitized subject after drug contact has ceased and time been allowed for excretion of the reaction products, all that remains is B If now A is given orally the reaction moves to the right then slows to equilibrium. With C and D slowly eliminated and A constantly given the reaction proceeds slowly to the right until B is exhausted and desensitization complete. In practice, each case is an individual problem but the greater the sensitivity the smaller the initial desensitizing dose must be and the more gradual the increments In very sensitive patients doses are covered by an *antihistamine No serious local or general reactions have* been encountered

For penicillin the initial dose is 50 units of crystalline penicillin G by mouth working up daily with early increments of 100-150 units/week, later increasing to a maximum of several thousand units daily over a period of 8-12 weeks. A test dose of 50 000 units three times in 1 day is then given followed in 10 days by a patch test Desensitization has been successful in seven of nine patients so treated.

Occasionally suspected sensitivity to penicillin is found due to the procaine radical Procaine an ester of para aminobenzoic acid, belongs to the large group of drugs with a primary aromatic amine structure which includes sulfonamides, para aminosalicylic acid and paraphenylenediamine many of which are known sensitizers Cross sensitization between members of this group is probably not uncommon. In patients sensitive to procaine cross-desensitization was attempted with sulfanilamide. Starting with 0 0625 Gm.

(9) Brit. J Dermat. 68:327 331 October 1956

also in relieving postherpetic discomfort in few cases when 3,000 µg. was given intramuscularly daily for three to four days. This treatment is less painful to the patient and much less expensive than immune globulin. In this connection it is important to realize that unless the therapeutic effects are regular and striking it is difficult to assess the value of therapeutic procedures in postherpetic neuralgias.—Eds.]

Treatment of Eczema Vaccinatum by Specific Gamma Globulin. Eczema vaccinatum following smallpox vaccination is a serious complication It s commonly seen in patients with eczema of a congenital ectodermal deficiency The mortality rate has been up to 40% Eczema vaccinatum was treated with accinia globulin by Max J Fox and Vincent B Pica (Marqu tte Univ)

Man, 57 with past history of an eczematoid eruption, had sever accinia following contact w th his daughter 18, who had had chronic eczema all her life and who received a smallpox vaccination about four weeks before, after which she developed generalized papulovesicular eruption. Temperature was 102.5 F Both anterior cervical and posterior auricular nodes were slightly enlarged, movable and nontender There were many vesiculopustular lesions on the face rms and chest some were excoriated. There was marked bilateral cellulitis. Conjunctivae were injected and a atery secretion was present in both intercanthal folds. Blood count was normal differential showed 55% segmented polymorphonuclear leukocytes, 21% stab forms, 15% lymphocytes, 2% monocytes and 7% eosinophils. Urinalysis, sedimentation rate and chest x ra were normal.

The patient was given 30 cc. vaccinia globulin intramuscularly His temperature shortly returned to normal, eczema improved rapidl and he remained stable except for one febrile episode.

Kempe bel eves that vaccinia immune gamma globulin is important in prevention and therapy of serious complications of smallpox vaccination and in smallpox pre ention in exposed susceptible contacts Vaccinia immune gamma globulin is a solution of globulin collected from donors who have been uccessfully accinated against smallpox from four to eight week before donation. This globul n may be obtained, free of harge, f om the Department of Pediatrics Uni er sity of California Hospital San Francisco Therapeutic dosage early cases of serious complications of mallpox va cination 0.3 cc./lb intram scularly When th total dose is greater than 10 cc it may be d vided and given t separate sites to reduc njection trauma. The exact prophylactic dose is undetermined 0.03 cc /lb is probably the minimal ef fecti e dose Doses of 0.06-0.12 cc./lb. would probably give

Wisconsin M J 5 972-976, September 956

ml 1 50 aqua ivy Excellent phylactic results were achieved in 49% good results in 43% and poor results in 8% of courses.

There was no evidence of nephritis or exacerbation of dermatitis in this series even when aqua ivy was administered to children as young as age 2 years. Current therapy of choice is hydrocortisone systemically for the acute severe case and aqua ivy for subsequent prophylaxis

► [This study carried out by an excellent group of investigators, once more demonstrates the immense difficulties involved in appraising the efficacy of prophylactic treatment in plant dermatitis. The authors themselves in their paper call attention to some of these difficulties. Among them is the fact that evaluation of results achieved was based on the patients own reports and on decrease in severity of the attacks rather than absence of attacks of dermatitis. The editors are of the opinion that the only reliable way available at present for establishing the efficacy of prophylactic treatment in poison ivy dermatitis is patch testing with serial dilutions of the allergen before and after treatment. Only if at least a quantitative reduction in patch test sensitivity is demonstrable can one accept the conclusion that the prophylactic treatment has had a beneficial effect.—Eds.]

Treatment of Herpes Zoster and Chicken Pox with Immune Globulin was tried by J G Rodarte and B H Williams[2] (Temple Tex.) in 11 patients with severe herpes zoster Prompt relief from pain was obtained and the skin lesions were modified Where paroxysms of lancinating pain occurred they did not recur after the first injection Immune globulin may possibly minimize posterior root ganglion and spinal cord damage and thus prevent postherpetic neuralgia. It is suggested that in herpes zoster 20 cc immune globulin should be given for four days 10 cc being injected high in each buttock daily

Since it is probable that herpes zoster and chicken pox are caused by the same virus 12 cc immune globulin was given daily for three days to five children with chicken pox beginning the first day the eruption appeared. Examination of skin lesions suggested that chicken pox could be attenuated in this manner

► [These authors report dramatic relief of pain, especially of shooting pains, following one injection of 20 cc. immune globulin in patients who received treatment *during* the acute period of the eruption Postherpetic pain apparently did not occur in these cases. Our own experience is limited to a case of severe postherpetic pain of six weeks duration in which it was doubtful whether any relief was derived from 20 cc immune globulin administered daily for four days.

We have had the impression that vitamin B may have been of some

(2) A.M.A. Arch. Dermat. 73 553-555 June, 1956.

haracterizes the L.E. cell requires cells L.E. gamma globulin and a factor present in both L.E. and normal serum that can destroy the intracellular inhib tor The present hy pothesis of the pathogenesis of the L.E. cell is that trauma to the cell in the presence of L.E. gamma globulin (which may be a antibody against mesenchymal cell membranes) per mits entry i to the cell of the normal serum anti nh'bitor wh ch destroys the nhibitor of DNase Thus DNase is free to cause nucleolysis (depolymerization of DNA)

The therapeutic application of the inhib tor seemed feasi ble, since it can traverse the cell membrane n both direc tions. Therapy consisted of administering 30 ml. freshly drawn heparinized blood from a compatibl donor intramu cularly three times weekly for several weeks, and then grad ually reducing frequency to very 10 days. Concentrated us-pension of leukocytes, normal or leukemic, also have been used Result were followed by observing the clinical course reversal of L.E. cell phenomenon and reduction n serum DNase activity

Report of 12 cases are presented. The results of hemoinoc ulation therapy were good in seven doubtful in two and poor in two One patient who was uremic before therapy was started died. Soon after beginning therapy serum DNase act ity was reduced in all patients. This is an effecti e guide to therapy it precedes the disappearance of L.E. cells and may on return to higher le els, presage a relapse Other changes noted i patients fter institution of therapy were clearing f cutaneous eruptions (n first week) subsidence of fever mprovement in arthralgias myalgias malaise, fat igabil ty serositis and urinary findings and disappearance of the L E. cell phenomenon (in three to six weeks) Bene-ficial result were noted on adding hemotherapy to steroid rout es a how by learing of previously uncontrolled ign a d ymptom and maintenance f improvement on reduced steroid doses Stero ds may inhibit the maximal ef fect f hemoinoculation by inhibiting the destruction of the inoculated leukocytes The hemotherapy procedure is quite saf lthough febrile reactions hav occurred on the first in jection Compatible blood i used to a oid the poss b l ty of majo blood group sensitization during prolonged therapy

Other therapeutic effects in lupus erythematosus may be

better protection This material should be given as early as possible after exposure to smallpox and should follow smallpox revaccination (given in at least two preferably three, insertions on the arm) by 12 24 hours Prophylactic use of this material in vaccination would be limited to children with eczema when a sibling is being vaccinated and household contact could be expected A child with eczema should never be vaccinated regardless of whether lesions are dry or wet

It is felt that this material has therapeutic value even when the disease is in its third or fourth day and it is probable that no further lesions will develop and that existing lesions will involute quickly

► [As has been known for many years, patients with atopic dermatitis are most susceptible to the vesicopustular eruptions which follow exposure to herpes simplex or vaccinia virus. It appears likely that atopic dermatitis was the underlying dermatosis in the patient as well as in his daughter

Dr C. Henry Kempe of the Department of Pediatrics, University of California Hospital, San Francisco, is quoted in the article as saying "Our purpose here is to invite others to contact us by telephone or telegram when such cases are encountered in clinical practice in contagious disease hospitals, in teaching centers, or in Health Department Well Baby Clinics. Upon such contact we will ship free of charge, by air express, the required amount of vaccinia immune gamma globulin for early use. There is, at present, not enough material available to allow us to send vaccinia immune gamma globulin to health departments for storage. —Eds.]

Rational Therapy of Systemic Lupus Erythematosus, based on observations of the L.E cell phenomenon is presented by N B Kurnick[4] (Univ of California, Los Angeles) Enzymatic nuclear lysis probably leads to formation of the L.E cell by depolymerization of desoxyribonucleic acid (DNA) These enzymes desoxyribonucleases (DNase) are found in serum and probably in all cells Leukocytes contain an inhibitor of DNase, a soluble protein with species specificity When added to normal leukocytes simultaneously with lupus serum the leukocyte extract containing the inhibitor of DNase prevents occurrence of the L E cell phenomenon indicating that the phenomenon occurs when the inhibitor is destroyed releasing the DNase from control with resultant lysis of the nucleus Leukemic leukocytes are richer in inhibitor than mature leukocytes Washing leukocytes enhanced nucleolysis on exposure to L.E serum by removal of inhibitor The production of nucleolysis which

(4) A.M.A. Arch. Int. Med. 97 562 575 May 1956

The problems i volved are illustrated by the following case.

Man, 23, in good health, was first vaccinated in 1945 without complications. Three weeks after revaccination in 1950, he had at the vaccination site an itching eruption, which spread to the shoulders and the chest. One week later lichenoid eruption was found round the accination site with a festoon-shaped extension to the anterior aspect of the thorax (Fig 1). The lesion consisted of miliary reddish brown papules, which on diascopic pressure



Fig Four weeks after vaccination. (Courtesy of Jorgensen, B B and Hervin, O Acta tuberc scandinav. 32 179 191, 1956.)

showed suggestion of transparency. A hazelnut-sized lymph node was found in the left axilla. After one week the eruption faded, and more distinct lichenoid appearance developed. The eruption subsided spontaneously during the following month.

The pathogenesis of these complications remains obscure.

► [The authors mention the following as possible factors in pathogenesis of the specific complications (1) dose and/or virulence of the vaccine, (2) technic of vaccination, (3) resistance of those vaccinated and (4) an allergic reaction. The fact that complications were more frequent and more severe in revaccinated persons lends weight to the role of an allergic mechanism.—Eds.]

Mepacrine in Rosacea was compared with standard routine of two doses of 70 r x rays at a nterval of 14 days and ightly use of a 2% ulf and 2% salicylic acid ointment for 4 weeks by Peter M I man and B Gordon. Mepacrine was

Acta dermat.-venereol. 35 446-453, 1 55

explained by the mechanism of cell destruction in systemic lupus which provides the rationale for hemotherapy. Steroids may exert a beneficial effect by (1) preventing reaction of the abnormal gamma globulin with the mesenchymal cell surface (2) inhibiting production of abnormal gamma globulin factor (3) lymphoclastic action, causing release of DNase inhibitor which is abundant in lymphocytes and/or (4) diminishing inflammatory reaction to cell destruction in the surrounding tissue. Quinacrine valuable in discoid lupus combines firmly with polymerized DNA in vitro and inhibits the L.E. cell phenomenon. This mechanism is different from that of DNase inhibitor which acts on the enzyme and not on the substrate. The results of the study were considered encouraging although caution must be used in interpretation of data because of the great variability in manifestations of the disease and occurrence of spontaneous remissions.

► [Kurnick here provides a clear and rational explanation of the pathogenesis of the L.E. cell phenomenon. The disappearance of the phenomenon and improvement of clinical signs of the disease following the therapy based on Kurnick's theory are impressive. The therapy however does not appear to be very practical and, even assuming the correctness of the theory unless more specific cellular extracts can be produced to destroy DNase inhibitor treatment of lupus erythematosus will continue to depend on ACTH cortisone and/or the antimalarial drugs. Of course, the ultimate goal remains, i.e. to find the etiology of the disease.—Eds.]

Dermatologic Complications of BCG Vaccination—150 specific and 16 nonspecific—were observed by B. Borch Jørgensen and O. Horwitz[5] (Finsen Inst., Copenhagen) among 100 patients. These were patients referred for treatment of sequelae of BCG vaccination i.e. a highly selected group of subjects. Specific tuberculous complications were subcutaneous abscess scrofuloderma lymphangitis local and universal tuberculid lupus vulgaris lupoid affection Koch's phenomenon, regional and universal adenitis. They generally followed a milder course. Among the nonspecific complications local eczema and keloid predominated. Complication were observed in all age groups normally vaccinated however lupus, lupoid affection and Koch's phenomenon were seen *only in* adults and universal tuberculids only in children. Complications were more frequent and severer among revaccinated persons than among those vaccinated only once.

(5) Acta tuberc. scandinav. 32 179-194 1956.

► [These favorable results must be considered in relation t the findings of Inman and Gordon, who compared mepacrine therapy with conventional treatment (see preceding article) Mepacrine, aralen[3] and related compounds have been shown to exhibit suppressive effect on member of inflammatory processes in the skin. Therefore, one cannot draw the conclusion that their beneficial action in rosacea is due to their interference with photosensitivity even if decreased photosensitivity is demonstrable in such cases.—Eds.]

Treatment of Polymorphic Light Eruptions with Chloroquine. Treatment of polymorphic light eruptions with mepacrine has been so promising that several workers have tried the elated substance, chloroquine, because the latter does not induce the yellow skin discoloration seen with mepacrine. The sk of patients with polymorphic light eruptions appears to differ from normal skin qualitatively and quantitatively Qualitat e differences are reflected by the characteristic eczematous and pruriginous eruptions observed in such pat ents after ultraviolet irradiation. Quantitative differences are seen in lack of adaptability to grow ng intensities f ultraviolet radiat on The latter appears n some degree to depend on the capacity of the skin to produce pigment.

Jørgen V Christiansen and Holger Brodthagen[4] (Finsen Inst Copenhagen) gave chloroquine diphosphate 250-500 mg daily to 58 patients with polymorphic light eruption. It kept about 75% free from symptoms and most of the others esponded favorably S de effects were blurring of vision and disturbance f accommodation dyspepsia and, n two patients, depigmentation of all scalp hair but these were sig nifica t ince all could be eliminated by dosage reduction or brief u pension of treatment Apart from transient methemoglobinemia, no blood changes were observed. A rise in minimal erythema dose could generally be demonstrated in patient in whom treatment was effect but not in those who howed no response. The effect of chloroquine on polymorph c light eruption is believed due to the ab l ty of this preparation t restore the adaptability of skin to ultraviolet radiat on.

► [There is increasing experimental evidence that chloroquine not only reduces ultraviolet erythema but certain other inflammatory reactions in the skin as well (see comment to next article) Also to be considered as an effecti contributing factor in reducing skin reaction to ultraviolet light is the thickening of the stratum corneum and, as mentioned by the authors, increased pigmentation hich is caused by the repeated irradiation. The

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[4] Brit J Dermat. 68 204 206, June, 1956.

administered in a dose of 100 mg three times daily for four weeks to 25 patients and the standard routine to another 25.

While the results from mepacrine were generally worthwhile they were distinctly inferior to the standard routine. There were no toxic effects from mepacrine other than skin discoloration and nausea. The drug was continued beyond the four weeks in eight of the less successful cases, and in five of these there was considerably more improvement than was noted at the first monthly assessment. Mepacrine might have given better results had the drug been maintained considerably longer than one month

► [Considering the side effects of nausea and skin discoloration, the remote chance of more serious drug reactions and the definitely inferior results from mepacrine therapy it appears advantageous in general to stick to the conventional forms of therapy for rosacea.—Eds.]

Mepacrine and Chloroquine in Treatment of Rosacea, regardless of its severity and duration but with reference to its possible provocation by light are discussed by Holger Brodthagen[7] (Finsen Inst. Copenhagen)

METHOD.—Moderate redness, pustules and infiltrations of the face were observed in 57 patients aged 14-87 whose chief complaints were itching and burning induced by temperature fluctuations and stormy weather Exposure to direct sunlight was provocative in 23. Mepacrine (100 mg.) was given to 21 patients and chloroquine (200 mg.) to 36. Dosage was 2 tablets daily for 10 days and then 1 tablet daily for at least 3 weeks. Maximum treatment with mepacrine was 10 weeks and 10 Gm. with chloroquine 15 weeks and 28.4 Gm. Patients were tested for light tolerance while not under treatment, using a mercury arc lamp with strong spectral lines of 2,970-3,020 3,130 A. on areas 1×1 cm. at 50 cm. for one two and four minutes.

Among the 57 patients infiltrations pustules and redness disappeared in 18. Telangiectasias were unaffected Another 10 reported improvement but without objective signs One patient had objective but no subjective improvement Of 23 patients who reported exacerbation by sunlight 16 improved. Side effects were greater in the group treated with mepacrine —yellow skin discoloration in 19 and seborrheic dermatitis in 2 9 patients had dyspepsia from use of chloroquine. No hematologic changes occurred Study of the minimum erythema dose was worthless

Patients who report sunlight as a provocative factor can be improved by agents which increase light tolerance and they should be used only in such cases

(7) Brit. J Dermat 67:421-425, December 1955

hagen) report on 97 cases of lupus erythematosus with the fixed type of lesion, discoid or erythematous. Dosages were 100 mg mepacrine twice daily for the first eight days, then 300 mg daily until yellow pigmentation became marked and subsequently 100-200 mg daily The most common total dose was 20 Gm., with a range of 1.6-49.8 Gm Observation from end of the first course of therapy was from 3 to 21 months (a erage, 9 7 months) Routine blood and urine tests to an ticipate side effects generally showed no change. There was no relation between sedimentation rate and therapeutic response There was no evidence that fixed lupus influences tuberculin sensitivity

Of 81 patient with discoid lesions, 22 (27%) had an excel lent esult, 34 (42%) improved and 25 (31%) were unchanged or showed doubtful effects. Of 16 with erythematous lesions, 9 (56%) had an excellent response, 5 (31%) improved d 2 (13%) were unchanged or had a doubtful response. About half the patients were treated in the hosp tal and half as outpatients there was little difference in results Sex and duration of the disease did not seem to affect the result of therapy although the incidence was three times greater in women. Prognosis was best in the older age groups. Of 16 patients over age 60, 6 (38%) had an excellent result, 9 (56%) improved and only 1 (6%) failed to improve. There were some ide effects dyspepsia in 16 (17%) dermatitis n 5 (6%) and disorders of sweating in 8 (8%) patients. No aplastic anemia was encountered. After treatment was stopped, most pat ents were observed for 12 months and about 80% relapsed, ndicating the effect is symptomat c rather than curati e. The mode of action of mepacrine could not be shown. Favorable esult m fi ed lupus erythematosus continued up to th use f a total f 25 Gm mepacrine higher doses gave no additional impro ement. Hope of improvement should not be bandoned until at least 25 Gm. has been used, nor n cases bown g early mprovement hould treatment be discontin ed until t least 25 Gm. has been admin stered. Greater fu tur use of chloroquine, which does not produce yellow skin pigmentation nd seems to ha e fewer ide effects is uggested.

► [See other articles for results with chloroquine and plaquenil —Eds.]

thickened horny layer of the skin is in itself capable of reducing the penetration of ultraviolet radiation.—Eds.]

Polymorphous Light Eruption Effect of Chloroquine Phosphate in Modifying Reactions to Ultraviolet Light. It has been reported that chloroquine phosphate suppresses polymorphous light eruptions but its mode of action is not known It has been suggested that chloroquine might act as a blocking or filtering agent for ultraviolet light. Milton M Cahn Edwin J Levy and Bertram Shaffer[9] (Univ of Pennsylvania) investigated its effect on the minimal erythema dose of hot quartz ultraviolet light in normal persons and in patients with polymorphous light eruption Its effect on other types of skin reactions including reactions to histamine, trichophyton filtrate and poison ivy antigen on normal skin, was also studied.

Chloroquine phosphate taken orally for one month had no effect on the minimal erythema response of the skin to hot quartz ultraviolet light in normal persons or in patients with the papular types of polymorphous light eruption. Neither did it alter the skin response of normal persons to histamine trichophyton filtrate or poison ivy antigen It did inhibit the papular response to hot quartz ultraviolet light in patient with polymorphous light eruption The study suggests that chloroquine produces its effect by modifying the reaction of the patient with polymorphous light eruption in a manner which suppresses the abnormal but not the normal responses to ultraviolet light in the sunburn spectrum.

► [These investigations of Cahn *et al* deal with one of the most intriguing questions in the field of dermatologic therapy today namely the mechanism of action of antimalarial compounds in lupus erythematosus, rosacea and other dermatoses. This work adds evidence that a seemingly obvious explanation not correct, i.e., that deposition of the drugs in the uppermost layers of the skin acts to filter out the effective rays of ultraviolet light.

It also confirms the previous work of Bettley and Page (Brit. J Dermat. 66:287, 1954), which showed that atabrine* does more than simply increase light tolerance and that of Blaich and Gerlach (Hautarzt 6:267 1955) who claimed an "antiphlogistic" effect on artificially produced cutaneous inflammations as well as other effects for these drugs. —Eds.]

Treatment of Lupus Erythematosus with Mepacrine Results and Relapses during Long Observation. Jørgen V Christiansen and Johs. P Nielsen[1] (Finsen Inst Copen

(9) J Invest. Dermat. 26:201 207 March 1956.
(1) Brit. J Dermat. 68 73 87 March, 1956.

skin to seven patients with chronic resistant lupus erythematosus. All showed considerable to complete involution of the lesions within two to four months of therapy The drug appeared to be at least as efficient as quinacrine or chloroquine and less toxic. It produced further improvement, sometimes substantial after the effects of sister antimalarial drugs had come to a standstill.

Woman, 33 had a patch of lupus erythematosus on the forehead and one near the tip of the nose, for almost three years. She was treated with quinacrine and chloroquine, with partial improvement. Plaquenil was then given orally—600 mg daily for one week, 400 mg a day for seven weeks and 200 mg daily for the following month. There was complete *involution* of the lesions. No signs of reactivation occurred during the following two months, with no therapy

Plaquenil[a] in Treatment of Discoid Lupus Erythematosus Preliminary Report. Despite the effectiveness of the antimalarial drugs quinacrine and chloroquine in discoid lupus erythematosus, many patients derive little or no benefit from them, often because of side effects compelling discontinuance of medication Henry M Lewis and Gerald M Frumess (Denver) tried a new synthetic antimalarial drug plaquenil, on 22 patients with a four month observation period. Patients whose disorder was under adequate control with currently available drugs and patients with systemic manifestations were not included. Topical medication consisted only of sun-screening preparations. Initial dosage was 400 mg after meals and at bedtime If this was tolerated and there was visible evidence of improvement, rapid stepwise reduction with a daily four dose schedule was attempted by omitting 200 mg every third to fifth day If signs of severe intolerance developed, the medication was abruptly discontinued until all side effects subsided and was then resumed by starting with 200 mg daily and increasing 200 mg every second or third day depending on therapeutic response.

A 50% improvement was achieved in 17 patients (77%) and 9 were free from all visible activity of the disease within an eight week period after plaquenil therapy was started. Every patient who could tolerate this medication improved some

Side effects varying from those severe enough to compel

[a] A.M.A. Arch. Dermat. 73:576-581, June, 1956.

Relapse in Discoid Lupus Erythematosus Treated with Antimalarial Drugs John Rogers and Owen A Finn[2] (Univ of St Andrews) reviewed their results in treatment of discoid lupus erythematosus with quinacrine and chloroquine with special reference to recurrence after end of therapy Most patients received 0 1 Gm. quinacrine three times daily for one month then 0 1 Gm twice daily for the next month and 0 1 Gm daily for the rest of the treatment Chloroquine was given on weekdays only The usual dose was 0.25 Gm. once daily but some received 0.25 Gm twice daily over a short period.

Patients who were classed as much improved and improved after quinacrine or chloroquine therapy all relapsed within one year to pretreatment status most became worse the following spring The type of the initial lesion did not appear to influence eventual response since of eight patients who remained clear after two years four had had infiltrated plaques with scarring and four had had the erythematous type Immediate results and number of recurrences after quinacrine and chloroquine were similar

Lupus erythematosus recurred in most patients within two years but if therapy was resumed the condition usually cleared again In some patients repeating the drug failed to control the condition and in these interchange of chloroquine and quinacrine usually produced either improvement or complete disappearance of the lesions. The high relapse rate does not minimize the usefulness of quinacrine and chloroquine, because further therapy with the same drug or change from one to the other usually produces the desired effect Relapse within one year suggests that this therapy is not curative but merely suppresses visible manifestations of the disease Therefore the authors maintain patients on a small dose for several months after apparent clinical cure

► [Once chronic discoid lupus erythematosus is brought under control and there is disappearance of active lesions, we try to gradually lower the dose over a period of several months. Our experience also shows a high rate of relapses and therefore it is often necessary to continue a maintenance dose, not only for months but for years.—Eds.]

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(2) A M A Arch Dermat. 74 387 388, October 1956.
(3) Ibid. 73 572 575, June, 1956.

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(2) A.M.A. Arch. Derma 74 387-388 October 1956.
(3) Ibid. 73:572 575, June, 1956.

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A M A. Arch Dermat 73 576-581, June, 956.

discontinuance of the drug to mild ephemeral reactions of questionable relationship to its ingestion, were observed in 15 patients (68%). No drug eruptions were noted nor were there changes in either the hemogram or the urine. Diarrhea occurred in seven patients and intestinal cramping pains in six.

Plaquenil® is beneficial to patients who have an inadequate therapeutic response to currently available medications and to patients who discontinue those medications because of intolerable side effects. In previously untreated patients it appears to produce more rapid clearing of visible lesions.

► [Our own experience with plaquenil® has shown it to be still another medication which may be used in the treatment of chronic discoid lupus erythematosus.

Like chloroquine it does not discolor the skin, nor have we seen any alterations in the white blood count after its use. We have not observed that plaquenil® is any more effective or produces fewer side effects than chloroquine. There are cases, however, which do better with one of these drugs than with the other.

When this drug was originally made available for investigative purposes in this country, the tablets were 400 mg. each; it has been placed on the market in 200 mg. tablets.—Eds.]

Comparison of Chloroquine and Gold in Treatment of Lupus Erythematosus was made by John T. Crissey and Philip F. Murray[5] (Buffalo). The study material comprised 90 patients with chronic discoid lupus erythematosus. Chloroquine diphosphate 0.25 Gm. three times daily for 14 days, two times daily for 14 days and once daily until remission or for at least 2 months, was given to 24 patients; 66 received gold sodium thiosulfate intravenously as follows: an initial dose of 0.025 Gm. with weekly increments of 0.025 Gm. until 0.1 Gm. per injection was reached. The 0.1 Gm. doses were continued weekly for 15-20 weeks.

No significant difference was found in the proportion of patients responding to these drugs, nor was there any detectable correlation between duration of the disease before and after treatment with either gold or chloroquine. However, patients receiving chloroquine responded more rapidly than those treated with gold. More recurrences were observed within a year after chloroquine treatment than after gold. No correlation was found in chloroquine-treated patients between the age and duration of the disease, but there was slight negative correlation after gold treatment. Visual

(5) A.M.A. Arch. Dermat. 74:69-72, July 1956.

disturbances and incubus but no serious side effects, were seen with chloroquine

It is felt that chloroquine is superior to gold esthetically and in ease of administration.

► [Not included in the data were fiv patients receiving gold and two receiving chloroquine in whom the drug had to be discontinued because of undesirable side effects This incidence ppears about equal for the tw medicaments

Those ho have used much gold in the past as treatment for chronic discoid lupus erythematosus are likely to have encountered far more serious side effects from the gold than they are now experiencing with chloroquine or the other antimalarials. While number of our patient hav had visual disturbances from chloroquine in doses of 0 5 to 0 75 Gm. daily do not recall any th incubus (nightmares) —Eds.]

Amodiaquin (Camoquin) in Treatment of Chronic Discoid Lupus Erythematosus Preliminary Report with Special Reference to Successful Response of Patients Resistant to Other Antimalarial Drugs. Robert B Pappenfort and James H Lockwood[6] tried amodiaquin on nine patients with chronic discoid lupus erythematosus. The starting dose wa 0.2 Gm. twice daily after one week t usually was reduced to 0 2 Gm. daily In som patients, a one week course appeared sufficient.

I nea ly all patients, response was dramatic Se en were intolerant of or did not respond to other treatment including quinacrine and hloroquine Only two patients had toxic reactions, consisting of nausea, diplopia and anorexia and both could resum treatment when dosage was reduced and then gradually increased. The toxic manifestations of amodiaquin reported by arious authors to include transient mild nausea, vomiting headaches diarrhea and a few other minor complaints, ar insignificant. The drug rarely f ever causes tanning of the kin or ti sues. It seems to produce mor rapid respo se than qu nacrine or chloroqu ne

Atabrine in Treatment of Lepra Reaction. Miguel Angel Gonzalez Prendes, Conrado Valhuerdi Fernández and Rogelio Cruz Báez[7] call attention to the fact that the lepra reaction, consisting of acute or subacut manifestations in the course of chro ic leprosy with exacerbat on of old lesions or appearance of new ones, dicates progression of the dis ease Unfortunately this reaction is often res stant to ther py The effects of atabrine on the lepra reaction were first

(6) A M A Arch Dermat 384-364, October 1956.
(7) Bol Soc cubana dermat 2 194 99 September 1955

observed in a patient in whom a reaction had been present for one month *despite previous treatment*. All medication was then suspended and atabrine® was given for control of intestinal parasites. Within 24 hours the patient's general condition improved. After a week temperature was normal, general condition was excellent with a gain in weight and skin lesions had disappeared.

These results led to clinical trial of atabrine® in 12 patients with lepra reactions. The daily dose was 0.3 Gm., divided in three tablets given for seven days. One patient was given 0.1 Gm. daily for a few days after completion of the seven day course. The response in all patients was excellent and in some spectacular. Fever and other general symptoms often were relieved within the first few days and skin lesions generally disappeared in about a week.

This small series does not warrant general conclusions, but the authors urge that others assay the therapeutic effects of atabrine® in the lepra reaction.

Action of Synthetic Antimalarial Drugs on Psoriasis. Synthetic antimalarial agents are effective against lupus erythematosus and some of the other light sensitive dermatoses through their capacity to screen out ultraviolet light. This reasoning led Theodore Cornbleet[8] (Univ. of Illinois) to question what would happen to diseases that benefit from exposure to ultraviolet light, such as psoriasis. Quinacrine, chloroquine and hydroxychloroquine were given simultaneously to six patients with generalized psoriasis. The dose of the first was 100 mg., of the second 250 mg. and of the third agent 200 mg., once daily.

The eruption in all became more acute and spread and in one patient developed into exfoliative dermatitis. After withdrawal of the drugs the skin improved distinctly to markedly and cleared entirely in two, but relapsed again after a varying interval. The antimalarials could again induce a recrudescence, but this second course took a longer time and larger doses. Presumably one reason the psoriasis flared under the influence of antimalarial drugs was that they screened out ultraviolet light. It is suggested, therefore, that persons prone to psoriasis should be exposed to much larger quantities of light than others for their *well being*.

(8) J. Invest. Dermat. 26:435-436, June, 1956

► [Prompted by the report of Ziprkowski, Halm and Bank (Acta Med. Orient. 13 45 1954) in which they first reported this unusual and characteristic response of psoriasis to tabrine,[6] the junior editor with Sulzberger presented patient with psoriasis who responded in the manner described abov (A.M.A. Arch. Dermat. 73:636, 1956). This reaction should be kept in mind whenever prescribing atabrine[6] or aralen to patients ith psoriasis.—Eds.]

Tetracycline Hydrochloride in Treatment of Acne Vulgaris, using an acne lesion counting system for control, is reported in 72 patients with typical acne by G A. Cronk, D E. Naumann E. J Heitzman F N Marty K. J McDermott and A. A. Vercillo[9] (Syracuse Univ) Observations were made on a triangular area of the cheek from the tip of the ea to the end of the nose to the middle of the chin All patients were given tetracycline hydrochloride 0.25 Gm orally four times a day until pustules had disappeared and no new ones appeared Then the dose was reduced to once or twice a day All adjunct e therapy was d sconti ued.

Reduction in the acne lesions for the group wa 50% in 30 days and 62% in 60 days. Seven of 72 patients failed to improve 6 remained static 1 became worse. If there was improvement, 33 patients had a 75% eduction in acne lesions n 30 days nd 21 had a 75% response after more than 30 day There was no correlation of clinical response with sensitivity of bacteria to tetracycline. Seven patients in the series had diarrhea during therapy which topped in five while therapy continued. Intercurrent ral infections occurred in 19 pa tients during the course of therapy The drug wa used on 43 patients for 60-272 days. No adverse reactio s were observed. Tetracycline in vivo may ha e pharmacologic actions other than t accepted a tibacterial effect.

► [In general, this study using method of counting the lesions on circumscribed area, confirms the results of others based on unscientific, old-fashioned clinical observation. It should be noted that in some patients striking improvement of acne vulgaris occurs after less than 30 days treatment ith broad spectrum antibiotics. Some of our own patients have improved markedly within tw weeks of such treatment.—Eds.]

Use of Tetracycline in Treatment of Acn Vulgaris Clinical Study W lliam C King a d M Allen Forbes, Jr (Uni of Texas) eport on 203 patients, aged 12-47 with acne vulgaris who were gi en t tracyclin for 1 18 mo th (average, 4½ months) The most difficult problems were determination of sati factory dosage and duration of treatment Daily

(9) A.M.A. Arch Dermat. 73 228-233 March, 1956
) South M J 49 873-879 August, 1956

dose varied from 100 to 1 000 mg In some instances, especially for patients on 750 mg/day the amount was later reduced to 500 mg or less Dosage which controlled the pustular element was the level considered desirable

Clinical appearance of the patient and the patient's opinion were criteria for evaluating effectiveness of treatment. Complete remission was achieved in 27 and partial but satisfactory improvement in 165 In both groups excessive skin oiliness and comedones required additional local therapy The only untoward side effect was mild diarrhea in seven persons

► [Our experience with the wide spectrum antibiotics over a period of years in pustular cystic and papular varieties of acne i similar to that of the authors. Our initial dose of tetracycline is usually 250 mg four times daily for four to seven days, after which the dose is reduced gradually provided the medicament proves helpful. When the lowest effective dose is ascertained, it s mai tained as long as is necessary sometimes months to years. As improvement continues, efforts are repeatedly made to lower the dose and discontinue the drug

The incidence of significant adverse reactions from these drugs in our series of acne patients has been practically nil This holds true for cases treated with the antibiotic alone in combination with nystatin, or with large doses of vitamin B complex. Even in patients who had to continue tetracycline or related drugs for months or years, none of the dire consequences which were feared might result from such prolonged administration have occurred

It is particularly i teresting that where the tetracyclines fail to control a troublesome acne, chloromycetin* in the same doses is often helpful. The possible hematologic effects of this drug however must always be kept in mind.—Eds.]

Mycostatin* Treatment of Monilial and Some Nonmonilial Dermatoses. Ch Grupper[2] (Paris) used mycostatin* (nystatin) in 60 cases of mucocutaneous and ungual moniliasis and in 95 dermato es not cau ed by Candida albicans. The drug was administered orally and/or topically The oral daily dosage given in four equal parts during 24 hours, was 1 tablet (500 000 units) for infant 2 tablets for children and 4 for adults Instead of tablets mycostatin* powder (3 500,000 units/Gm) may be mixed with food or dissolved in beverages Dermatologic preparations included ointments (5 000-10 000- and up to 100 000 units/Gm of excipient e g plastibase* Squibb carbowax* propylene glycol lanolin petrolatum and others) freshly prepared lotions (5 000-10 000 units/cc. propylene glycol) mouth wash gargle containing 3 tablets of 500 000 units dissolved in 30 cc glycerin

(2) Semaine hop. Paris 32 2253-2263 June 30, 1956.

borate mouth wash, and aqueous suspension (2 tablets in 40 cc. water) for vaginal tampons. For gynecologic purposes also glycerin vaginal tablets of 250 000 units each were used.

In mucocutaneous moniliasis (perlèche glossitis stomatitis anoperineal and vulvovaginal infection due to C. albicans, balanitis with or without balanoposthitis and intertrigo of large folds) local treatment was usually sufficient. In ungual moniliasis (nail involvement with or without paronychia) mycostatin* proved to be fast-acting and specific particularly when combined with abrasion of infected parts of nails. For superficial mucocutaneous moniliasis, topical and oral administration of mycostatin* were combined in a single case. In the rare, deep granulomatous verrucous vegetating generalized type of moniliasis corticotherapy was added to combined oral and local mycostatin treatment.

In the nonmonilial dermatoses in which mycostatin was administered internally or topically to change the intestinal or surface flora, results were varying. In some cases of pemphigus psoriasis parakeratoses, pustular bacterid and pyodermitis of infants the response was favorable.

Mycostatin was well tolerated by all patients. It proved to be most effective in treating C. albicans infections.

* [Little doubt remains as to the therapeutic effectiveness of nystatin (mycostatin, Squibb) in the management of certain monilial (C albicans) infections when used locally on the infected part. We have not seen beneficial results achieved through the *oral* administration in the treatment of such common dermatoses as monilial paronychia, intertriginous moniliasis, etc.

In our own experience, there have been no allergic contact sensitivities to this product. On the other hand, mycostatin* in plastibase is not always well tolerated in certain intertriginous spaces, e.g., the genitocrural folds.—Eds.]

Progressive Bacterial Synergistic Gangrene: Report of Case Treated with Chloramphenicol is presented by J. Graham Smith, Jr. (Duke Univ.). Progressive bacterial synergistic gangrene usually begins postoperatively in the skin around retention sutures after drainage of a peritoneal abscess or empyema, or around a colostomy ileostomy after a trivial superficial accidental wound and in a long-standing skin lesion. Pain and tenderness of the lesion are usually present but fever anemia and prostration are unusual. Although the lesion has a characteristic appearance other chronic gan

[1] Am. Int. Med. 44: 607 1015 May 1956

grenous processes e.g. pyoderma gangrenosum (gangrenous impetigo) fusospirochetal infection and amebiasis cutis must be considered as well as cutaneous leishmaniasis, cutaneous diphtheria blastomycosis bromoderma and tuberculosis verrucosa cutis There is a central granulating ulcer of shaggy consistency which may become bright red and clean later Destruction of the dermis is not always complete islands of epithelium may regenerate from hair follicles and sweat glands

The periphery of the ulcer may show slight undermining A 1-4 cm wide rim of grayish brown gangrenous skin resembling suede leather surrounds the ulcer This merges with an elevated purplish zone peripherally which, in turn, coalesces peripherally with a 1 10 cm area of erythema which fades into normal skin

The treatment of progressive bacterial synergistic gangrene has not been satisfactory Surgical extirpation of the affected areas and local antiseptics were the earliest therapy used. Penicillin has been effective in some patients, but parenteral bacitracin has been the therapy of choice The author reports successful treatment with chloramphenicol in a patient with this type of gangrene produced by microaerophilic nonhemolytic streptococcus and Aerobacter aerogenes

Woman, 32, had a papular lesion on the right lower leg after slight trauma, which rapidly progressed to a vesicular and later to a larger bluish, bullous lesion. For 11 days, oral cortisone penicillin, oxytetracycline and various topical medications were given, with progressive enlargement of the lesion. She was febrile but had no systemic symptoms.

General physical examination revealed no abnormalities. There was a 10×16 cm. purulent, necrotic ulcerated, tender lesion involving the anterior tibial area of the right lower leg The ulcerated area was encircled by loose redundant skin attached peripherally to an edematous, well demarcated, purplish zone. There was moderate right inguinal adenopathy

The leukocyte count was 31 000 with 77% polymorphonuclears and 6% stab cells. The Schick test was markedly positive with a slough A biopsy revealed pseudoepitheliomatous hyperplasia. A microaerophilic nonhemolytic streptococcus and A. aerogenes were grown.

After penicillin streptomycin, sulfisoxazole systemically and prophyllin* and gentian violet locally had failed, chloramphenicol, 500 mg four times daily was initiated. Within three days the temperature fell below 100.4 F Two weeks later when the drug was discontinued for 1½ days, exacerbation occurred. Readministration

of the drug brought improvement altogether 66.5 Gm. chloramphenicol were given in 35 days. Local measures included 0.25% silver nitrate and 0.5% hlora dine T compresses to control the secondary invaders. With animal inoculations, the synergistic etiologic agents were shown to be a microaerophilic nonhemolytic streptococcus and A. aerogenes.

► [It should be emphasized that the dose of chloramphenicol used in this case as 2 Gm. daily This dose is about twice the amount usually administered to control infectious disorders. One cannot tell from the data given hether equivalent doses of penicillin and oxytetracycline were used and thus hether the failure of these antibiotics was the result of lack of effectiveness or inadequate dose.

Our own experience suggests that starting patients on doses of antibiotics greater than those now accepted as routine initial doses (g 1 Gm. daily of tetracycline or chloramphenicol) will sometimes make the difference between success and failure in the management of certain inflammatory lesions.—Eds.]

Note on Natural History of Lichen Planus. Peter D Samman (Westminster Hosp London) treated some patients with li hen planu w th standard methods and compared their progress with untreated controls The first group wa treated with acetarsone (1 gr daily by mouth) and the second group with mercury (60 minims solution of mercuric chloride three times a day by mouth) Two out of thre patient were gi en on o th other drug and the third a bland substitute All were gi en soothing local pplications, and when irritation was severe, phenergan o a barbiturate was added.

Of 121 pat ents, mucou membrane lesions were present in 77 % and nail changes n 9% The latter varied from a d ffuse pitting ertical ridging to complete na l destruction The most characteristic cha ge was a thinning of the nail plate followed by an overgrowth of the cuticle to form a mantle wh ch covered a considerable portion of the nail. Shedding of the nail may be permanent or the nail may part ally regrow (Fig 2) Often when the nail was involved there were papules of lichen planus on the dorsum of the distal phalanx close t th nail In this series no alopecia was seen. \ tiligo was found in association w th lichen planus in four patients. Although some patients showed anxiety or other nervous tra t and n a number of instances emotional factors precipitated the disease, these factors were un mportant

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Brit J Dermat 68 73-181 May 1956

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phenylbutazone was confirmed by the following facts consistent and prompt effect on pruritus, disappearance within the first 10 days of plaques which had persi ted unchanged for months rapid and permanent disappearance of elements which remained after classic treatment and reappearance of pruritus and infiltration when treatment was stopped early

Although dosage may be adjusted individually experience suggests the following regimen 0.8 Gm. daily for three days 0.6 Gm for three days and then 0 4 Gm. daily which is usually sufficient for maintenance therapy Phenylbutazone is usually well tolerated if there is no sign of leukopenia and the patient is instructed to stop medication and report any s gns of toxicity Dose of 0.4 Gm. daily can be gi en for a month with intermissions of one week between courses. In two cases dosage had to be increased to obtain satisfactory results and in three, the drug had to be suspended because of leukopenia. When a lowered leukocyte count i restored to normal, treatment can be safely reinstated. Appearance of leukopenia seemed to coincide with maximal effecti enes of phenylbutazone For patients pred sposed to a toxic reaction because of hypersensitivity or other conditions it is best to begin with a small dose (0 1-0.2 Gm.) increasing gradually to the recommended therapeutic dose Result with phenylbutazone in chronic lichen planus suggest that at present it the treatment of choice

► [The question is whether in such benign dermatoses as lichen planus, one is justified in using form of therapy no matter how effective, when it produces leukopenia in three of series of ten cases —Eds]

Lichen Planus Clinical Study of 67 Cases with Results of Penicillin Therapy is presented by S. C. Desai and L. Marquis (KEM Hosp., Bombay) Most of the 58 males and 9 females were the 20-40 ear age group There were 29 cases of hypertrophic lichen planus, 22 of lichen planus pigmentosus sine lichen, 6 of acute generalized lichen planus and a few each of mucosal annular linear m ltisegmental linear and follicular types. The disease bore no relation to drugs dietary habits, occupation o other constitutional diseases, or to social class Res lts of histologic stud es were all typical of lichen pla us, cept for th pigmentary type, in which the basal layer had markedly increased melanin and the dermis an increase in free melanophores.

) Indian J Dermat & Venereol 22 33-41, Jan Mar 1956.



Fig 2 (Courtesy of Samman P D Brit. J Dermat 68 175-181 May 1956)

tivity 23% were clear within six months and 64% within a year Recurrence was noted in 20% of patients

► [Cortisone treatment, not included in this series, would be expected to produce favorable results in some cases —Eds.]

Phenylbutazone in Treatment of Lichen Planus was effective in 9 of 10 cases studied by Alberto J Melamed[5] Therapeutic action of the drug was directly proportional to age of the lesion It was less efficacious in acute cases Some lesions and sites apparently were more resistant but eventually were controlled e g the active border surrounding certain plaques keratotic residue following disappearance of certain plaques and mucous lesions which vanished or diminished some time after clearing of cutaneous lesions Lenticular papules were moderately sensitive and recent micropapules were irregularly influenced Pruritus was relieved in all cases, including the one classified as a failure usually in 48 hours after start of treatment The effect on pruritus appeared to parallel that on infiltration since when the drug was suspended both reappeared simultaneously

That the observed improvement was specifically due to

(5) Arch. argent dermat. 5 321 327 December 1956

and phenergan,* acute intoxication with alcohol or hypnotics, and icteric and circulatory symptoms (except tachycardia). Side effects are sleepiness, tachycardia, dizziness and urticarial eruptions. Icterus or parkinsonism was not seen.

Serpasil* is an alkaloid of Rauwolfia serpentina. Until sedative effects are produced initial doses of 7.5-10 mg are administered intramuscularly, followed by oral doses (maximal daily dose, 6 mg) with subsequent gradual reduction to maintenance dose of 1-1.5 mg/day. The latter can be continued for one to four months. Side effects include rhinitis, conjunctivitis and acute excitation.

Chlorpromazine and serpasil were used in chronic eczema, neurodermatitis (particularly of the disseminate type), lichen ruber and psoriasis vulgaris. Sedation therapy with chlorpromazine (alone or combined with phenergan) was often beneficial. Subhibernation therapy with chlorpromazine was quite effective in cases in which psychic changes prevailed. In these, general rest and the change in the psychic condition had an indirect healing effect on the dermatosis. Chlorpromazine also achieved complete cure within a short time in seven of eight cases of prurigo simplex chronica, and (combined with cibalgine) caused marked improvement in two cases of neuralgia following herpes zoster. Antipruritic effects were seen after chlorpromazine administration and less constantly after serpasil.* In nocturnal pruritus with disturbed sleep a "cocktail" of 2 tablets of chlorpromazine (25 mg each) combined with 1 or 2 tablets of phenergan (25 mg each) or 1 or 2 capsules of benadryl* (25 mg each) and possibly 0.1 Gm. phenobarbital had good effects.

► [As pointed out in the leading article of this YEAR BOOK, the high incidence of cross-sensitization between chlorpromazine and phenergan should constantly be kept in mind. This applies not only to allergic eruptions resulting from systemic use of these drugs, but from external contact as well. In addition to the contraindications mentioned, it should be remembered that instances of jaundice due to cholangiolitis and even rare cases of acute hepatitis and hematopoietic difficulties have been reported following the use of chlorpromazine.

It is obvious that the modern tranquilizing drugs such as chlorpromazine, rauwolfia alkaloids, promazine, meprobamate, etc. have certain distinct advantages over the older barbiturates, salicylates, avertin, chloral hydrate, etc. Nevertheless, pretty much the same effects could be achieved with these "old fashioneds" as with the new "cocktails" described in this article.—Eds.]

Penicillin therapy was used in three different regimens (1) 600 000 units of PAM daily or every other day to a total of 6 000 000 units (2) the same but supplemented with 600 000 units of diamine penicillin weekly for 10 weeks to a total of 12,000 000 units (3) diamine penicillin in doses of 600 000 units per week for a total of 6 000 000 units. Patients were considered cured 75% relieved 50% relieved and with poor results

Regimens 2 and 3 showed better results in all groups, with at least 50% improvement. Poor results in general were seen in the pigmentary group In comparison with heavy metal therapy the results appeared to be about twice as good with penicillin The results warrant further investigation of this method of treatment

Largactil and Serpasil ***in Dermatology*** are discussed by U W Schnyder and R. Schauwecker[7] (Univ of Zurich) Two additional recent drugs largactil (chlorpromazine) and serpasil * can be used in pruritic dermatoses together with sedatives calcium parasympatholytic and sympatholytic drugs and antihistamines (sedation therapy) They are also useful in long lasting refractory pruritic dermatoses, with bodily and mental exhaustion and marked insomnia. In the latter group both drugs can be used in a modification of treatment that causes sleep or prolonged somnolence (subhibernation therapy)

Chlorpromazine is a phenothiazine derivative and has sedative effects that increase those of hypnotics analgesics and antihistamines and also has antipruritic action In chlor promazine subhibernation therapy in excited or depressed patients initial dosage is 300-600 mg (oral and rectal doses combined) After 10-14 days tablets only are given and doses are gradually reduced to a maintenance do e of 50-150 mg which is continued for 20-60 days. Pulse temperature and blood pressure must be checked and urine examined twice weekly for urobilin and urobilinogen In chlorpromazine sedation therapy within a week the initial dose of 25 mg is gradually increased to 100-150 mg This maximal dose is continued for 10-14 days and afterward slowly reduced to maintenance dose (50-150 mg) Contraindications to chlor promazine include eczematous eruptions from the drug itself

(7) Dermatologica 111 185-197 October 1955

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and chondroitin sulfuric acid. These two mucopolysaccharides are inactivated by the enzyme hyaluronidase with resulting increased permeability and changes of viscosity. Heparin, in addition to its effect on blood clotting, fat metabolism and the adrenocortical system, has an inhibiting effect on hyaluronidase. Because of this inhibiting action it has been used in the treatment of pemphigus vulgaris. However the results thus far have not been uniform. A case is reported in which remission were achieved only by intravenous administration of heparin; other observers have given it intramuscularly.

Woman, 36, was given heparin (*liquaemin*®) initially in relatively small doses (60,000 heparin units); dosage was decreased rapidly to 40,000 and 20,000 units, then increased when new eruptions appeared after intramuscular depot injections of heparin. No evidence of intolerance, particularly allergic reactions, was observed. Occasionally mild nausea or tachycardia occurred after the injection. Thorough checking of blood coagulation was done at regular intervals. Treatment lasted only five months, because the patient died of recurrent cervix carcinoma.

A second patient, with dermatitis herpetiformis, had a paradoxical reaction to the hyaluronidase inhibitors suramin and heparin (220,000 units of liquaemin within four days), the administration of either drug being followed by intensive bullous eruptions.

Acrodermatitis Enteropathica (Danbolt-Closs) in Five Siblings: Efficacy of Diodoquin in Its Management. Acrodermatitis enteropathica is characterized by alopecia of the scalp, eyebrows and eyelashes, with associated photophobia. The typical eruption (Fig. 3) occurs as irregularly shaped vesiculopustulobullous plaques located chiefly around the mucocutaneous orifices and on the peripheral areas of the extremities. The distal phalanges show severe paronychia; the nails are often distorted and sometimes even lost. During exacerbations, the cutaneous lesions appear quite inflamed. The tongue and buccal mucosa show a whitish coating with associated halitosis. In addition to the skin findings, the infant with the well developed disease presents the typical picture of the celiac syndrome. The patient is listless, anorexic and apathetic. There is tissue wasting and retardation of growth. The disease is noted for periods of spontaneous remission and exacerbation and has a high morbidity and mor-

Treatment of Pemphigus with Potassium Para Aminobenzoate C J D Zarafonetis A. C Curtis and J M Shaw[8] treated 18 patients suffering from various forms of pemphigus with potassium para aminobenzoate (KPAB) usually administering 30 ml (3 Gm) of a 10% aqueous solution every three hours for six to eight doses or a total of 18-24 Gm. daily Duration of therapy varied from a few weeks to more than two years

All eight patients with pemphigus vulgaris who received KPAB therapy for over a month had marked to complete suppression of the disorder Pemphigus foliaceus responded incompletely although two of four patients improved well clinically Pemphigus erythematodes cleared completely in one patient fairly well in another and only slightly in a third. The only patient with ocular pemphigus showed definite improvement. Gratifying results were obtained in three patients treated with both KPAB and cortisone after large doses of steroid therapy alone had failed to control the disease satisfactorily

In several patients whose disease was completely suppressed KPAB was stopped and they were observed for relapse. Two have remained in remission for over two years and others have relapsed and died while under different treatment elsewhere The only potentially serious complication of KPAB therapy is hypoglycemia This may be prevented by interrupting therapy if the patient fails to eat. The drug may be resumed as soon as the patient is again eating normally

The mechanism by which KPAB exerts its effects in pemphigus is not known It must act at a fundamental metabolic level to modify the manifestations of pemphigus scleroderma, dermatomyositis and a variety of other disorders It is felt that KPAB alone or in combination with steroid hormones offers a valuable adjunct to the management of several forms of pemphigus

Heparin Therapy in Pemphigus Vulgaris is discussed by W Meyhofer and F K. Beller[9] (Giessen Germany) Intracellularly the skin consists of acid mucopolysaccharide the largest and most important part of which are hyaluronic acid

(8) Am. J M Sc 231 30-50, January 1956.
(9) Hautarzt 7:78 82, February 1956.

toms disappeared. If the drug was stopped for as long as three days during an exacerbation period, all symptoms promptly reappeared. Two patients received the drug for almost two years without any side effects.

► [In some cases diodoquin is said to have been unsuccessful or only partially successful in controlling acrodermatitis enteropathica.—Eds.]

Lupus Vulgaris Treated with Isoniazid Present Status of the Disease. Brian Russell and N A. Thorne[2] (London Hosp.) report four years experience with isoniazid treatment of 111 patients with lupus vulgaris. All 103 patients who completed the course of treatment improved In 99 the lesions cleared clinically The latter were followed for 6-24 months after completion of the courses. Relapses (with solitary or grouped nodules) occurred in 11 in whom average length of treatment was 32 weeks and average total dosage of isoniazid 79.5 Gm. In 88 patients without relapses, average length of treatment was 46 weeks and average total dosage was 108.5 Gm In nine of the patients with relapse the lesions again cleared with various treatments, and two were improving on a second course of isoniazid.

The suggested dose for adults is 300 mg isoniazid/day for at least three months after clinical clearance. This usually entails a year's treatment with total dosage of about 110 Gm. A daily dose of 400 mg did not produce earlier clinical clearance.

Isoniazid was effective in a patient with tuberculosis verrucosa cutis, in three with scrofuloderma and in two with erythema induratum, but not in one with lupus miliaris disseminatus faciei.

Response of Chronic Nonspecific Urticaria to Plasma Cholinesterase is reported by Orman Gregersen (Hollis, N Y) and Robert D B rnard[3] (Laurelton N Y) Recurrent urticaria unrelated to allergy but evoked by stress situations has been called cholinergic urticaria. It is believed to be associated with diminished cholinesterase level of the plasma. Substitutive increase in plasma cholinesterase is now possible because the plasma enzyme is available in concentrated form

CASE 1—Man, 29 had had daily recurrent giant urticaria for six years. Penicillin or sulfonamide sensitivity was not evident, and response to antihistamines and cortisone was insignificant. The

(2) Lancet 2 908 11, Oct. 30 1954.
(3) New York J. Med. 54 1459 1461 May 15, 1954.

tality rate if not diagnosed and treated properly. During exacerbations growth ceases. Diodoquin* (diiodohydroxyquinoline) has been found to control completely all manifestations of the disease.

James S. Vedder[1] (Marshfield, Wis.) describes five sib-

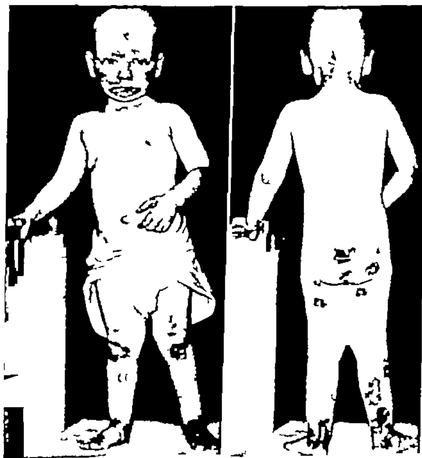


Fig. 1.—Characteristic distribution of cutaneous lesions of acrodermatitis enteropathica. Note alopecia and pathetic facial expression. (Courtesy of Vedder, J. S.: J. Pediat. 48:212-219, February 1956, from Dillaha, C. J.: J.A.M.A. 152:509-512, June 6, 1953.)

lings with acrodermatitis enteropathica. The occurrence of five cases in the same family supports the belief that acrodermatitis enteropathica is a familial hereditary disease. All five patients had few symptoms while on breast feeding. When diodoquin* was given over two or three weeks, symp-

(1) J. Pediat. 48:212-219, February 1956.

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(2) Lancet 2:808-811, Oct. 20, 1956.
(3) New York J. Med. 56:1439-1441, May 15, 1956.

facial lesions improved the day after intravenous injection of 2 cc. cholase (human plasma cholinesterase preparation containing 350 Hink units/ml.) A second injection of 4 cc. 24 hours later resulted in clearing of all lesions, and he has been clear for one month. The therapeutic response persisted beyond the period of presumed rise usually only four days.

CASE 2.—Woman 37 who had had Hodgkin's disease for six years and had received oxytetracycline and cortisone for three years, for four months showed recurrent giant urticaria, provoked by scratching a moderate daily recurring pruritus. After injection of 2 cc. cholase, the urticaria disappeared in 48 hours with no reappearance during the subsequent 4 weeks.

The nature of the response did not serve to differentiate the mode of action between that of specific enzyme substitution and that of nonspecific effect i.e. foreign protein reaction.

Vitiligo Treated with Chloroquine. Preliminary Report by *Jorgen Christiansen*[4] *(Copenhagen) indicates that light sensitivity of depigmented areas was reduced and that increased light tolerance was followed by diffuse repigmentation which resembled that following treatment with the psoralens in requiring exposure to ultraviolet radiation and occurrence in perifollicular ephelis like patches.*

Man 49 had vitiligo patches on the thighs since age 12, which later spread to trunk face neck and arm until about 75% of the entire skin surface and 90% of the face were depigmented. Strong sunlight while yachting had caused redness, itching and edema of the exposed areas. After one week of treatment with 500 mg chloroquine daily he tolerated exposure without inconvenience. After one month the dose was reduced to 250 mg daily because of diarrhea, but light tolerance remained unchanged. After a month's cruise in the sun ephelis-like perifollicular patches of repigmentation which later fused were seen on the face. Repigmentation also occurred on trunk and extremities after sun bathing. On the back of the hands, previously depigmented hairs reassumed a dark blond color. Four months after treatment began there was repigmentation of about 50% of the skin surface and about 90% of the face. Total dose of chloroquine was 30 Gm.

► [Is the repigmentation in this case the result of a combined action of the chloroquine and sunlight on the melanocytes or is it the result of the increased tolerance to sunlight, made possible by the chloroquine, thus permitting prolonged exposure and adequate stimulation of the melanocytes to produce pigmentation? According to the concept of Jarrett and Szabo, the vitiligo in this patient might be classified as relative type I or relative type 2.—Eds.]

Effect of Vibra Puncture into Areas of Vitiligo. David Grinspan, Ricardo Calandra and Jaime Fairman[5] (Buenos

(4) Acta dermat venereol 35 453-456, 1955.
(5) J. Invest. Dermat. 26 243-246, April, 1956.

Aires) treated vitiligo in 107 patients by mechanical excitation of the lesions produced by superficial penetration of the skin with the needles of a tattooing apparatus. Forty six patients received sufficient treatment for evaluation. Satisfactory results were achieved in almost half of them. Better results were obtained when gold, in oil suspension, was applied before use of the needles. The irritation caused by the needles is considered to be the main factor in the production of the pigmentation.

The best clinical response was obtained on the face. Failures were observed mainly on fingers and toes. Pigmentation appears slowly usually after 15-20 weekly applications. Most patients, after three years of treatment, showed no evidence of recurrence.

Histologic studies revealed the presence of true melanin in the treated areas. In two patients, new lesions appeared *during treatment in others, true pigmentation was observed* in areas which did not receive treatment.

► [The number of cases successfully treated in this series (48% considered cured and 22% improved) is much higher than in most series reported of patients treated with 8-methoxypsoralen applied externally and taken orally in combination with ultraviolet light or sunlight. In order to permit more accurate evaluation of vibropuncture therapy it would be helpful to know after how many treatments the 35 patients, not included in the authors' statistics, discontinued therapy In future reports on the management of vitiligo it would be desirable also to give more details on the skin color of the patients treated. It appears that the results of therapy are likely to be better in dark skinned persons than in those with fair skin —Ed.]

A Few Observations on Leukoderma and New Method of Treatment are presented by A. A. Carvalho[4] (Ahmadabad India) who noted that the ffectiveness of remed es used in this disease varied directly with the amount of erythema and blistering that followed their use. There was no response to liquor epispasticus in six patients to local intradermal injection of 0 1% histamine acid phosphate n x or to injections of 10% cetylchol e, with r without exposu es to ultra iol t light in six others. Croton oil was applied once daily to patch u til an nflammatory reaction was obta ned. After inflammation had subsided, the o l was eappl ed Some pat ents ecei ed suberythema exposu es to ultraviolet l ght twice weekly

The dev lopment of pigment was most noticeabl t the hai follicles d sweat pores The most rapid epigmenta

4 Indian M. A. 26:93 96, Feb. 1 1956

tion occurred in patients who had the most rapid inflammatory response to croton oil. Repigmentation was always preceded by erythema with or without vesication and occurred sooner when combined with ultraviolet radiations. Both croton oil and ultraviolet light produced a greater inflammatory reaction in normal skin than in leukodermatous skin that is blistering occurred more readily at the pigmented borders than in the patches themselves. Croton oil must be handled carefully because of its toxic systemic effects and its strong counterirritant properties especially on normal skin.

Of 106 patients with leukoderma 81 were given a trial with various counterirritants and vasodilators. Three were treated with croton oil alone and 57 with croton oil and ultraviolet light. Two normal persons were treated with croton oil and showed erythema and vesiculation but no change of pigmentation With croton oil and ultraviolet light treatment the earliest signs of repigmentation occurred in 11 days The skin regained its normal color in 65.3% of the patients who were presumed to be cured

Of the counterirritants tested croton oil seemed the most effective in producing repigmentation in leukoderma. That leukodermatous skin does not react to croton oil or ultraviolet light as readily as normal skin suggests that melanin does not necessarily protect the skin against ultraviolet light and that the derangement in leukodermatous skin may not be confined to a disturbance of pigment formation alone

► [That normal pigmented skin tolerates less ultraviolet light than leukodermatous skin is indeed contrary to conventional thinking A cure rate of 65.3% in leukodermas is exceedingly high. As has been pointed out in the editorial comment to the preceding article, persons with more pigmented skin (in this case Indians) apparently respond much better to treatments for vitiligo and other leukodermas than fair skinned persons. —Eds.]

Corrective Dermatology IV Report on Treatment of Freckles with Phenol-ether is described by Renate Schuhmachers Brendler[7] (Univ of Munich) The method of phenol-ether therapy worked out by L. Winter was used in 51 patients. In children and frail persons the area to be treated was reduced the face was treated in two or more sessions and treatment areas in other regions did not exceed that of the face. This precaution was taken to avoid the often reported toxic symptoms of dizziness tinnitus malaise and

(7) Hautarzt 6:499-501 November 1955

tachycardia. Burning sensations beginning a few minutes fter treatment was started and lasting about one hour were followed by minor pains that continued several hours but were never unbearable. Analgesics therefore were not needed. Post-therapeutic observation time wa about two years, but even d ring this comparati ely short period recurrences were seen. Treatment was repeated in such cases and usually was successful. The tendency to recurrences apparently depends on indi idual d sposition to pigmentation and on intensity of freckling but even if there are recur rences, the n mber and intensity of freckles are greatly reduced Recurrence was observed in about 30%. Occasionally irregular pigmentation appeared n treated areas a few weeks after treatment particularly in the shoulder and upper arm regions of dark-pigmented persons but disappeared within six months For this reason test treatment of a small area is recommended.

► [It should be noted that phenol, under the conditions of use described here, can cause pallor, malaise, tachycardia, etc., and when applied to larger areas, has been known to cause sudden death. In iew of this and the reported recurrences in 30% of treated cases, one would hesitate to employ this form of therapy for harmless cosmetic defect, especially in children.—Eds.]

Treatment of Cheilitis Exfoliativa of Lower Lip with Hyaluronidase Report of Four Cases. The treatment of cheilitis of the lower l p is often d fficult. Patient usually wait until the process is d anced, a d considerable self-treatment has failed when seen, the condition is usually chron c Its cause is unknown. Osw ldo Ramirez C (Hosp Rosales, San Sal ador) reports result obtained w th injections of hyaluronidase fou patients w th chronic cheil t s xfoliati a who failed to improve w th a ariety of med catic n both sy temic and topical

TECHNIQUE.—Hyaluronidase equivalent to 150 USP (turbidity reducing) units is diluted in 1 cc of 2% solution of procaine and administered with small hypodermic needle, on plane parallel ith the lip surface. A drop is injected at the point of entrance of the needle following which the needle is ntroduced into the lip 1 cc is injected as the needle is w thdrawn I jections are distributed so that the whole diseased area is infiltrated. The pain produced by the first dose gradually diminishes as the induration lessens. Treatments re repeated twice weekly up to six weeks. An ointment containing hydrocortisone with neomycin (1%) wa used

J Invest Dermat. 26:343-345, May 1956

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(7) Hautarzt 6 499-501 November 1955

whether this is a primary or secondary involvement. The usual cause is an infection. Paronychia is frequently found in patients with vascular abnormalities of the extremities such as chilblains and in those whose work involves exposure to water and detergents. There is frequent association with sepsis elsewhere in the form of boils or abscesses.

The aim of treatment is to (1) keep fingers dry (2) sterilize the pocket under the nail fold by pushing a wisp of cotton soaked in pure phenol into it for about a minute once a week and then having the patient paint around the nail at night with some antiseptic, such as 0.5% bichloride of mercury and 0.5% brilliant green in alcohol (3) restore the anatomic contour so the nail fold can again adhere to the nail and (4) improve, if possible, the circulation of the fingers. Still better results are obtained using 100-150 r of superficial radiation. A plastic seal over the nail fold helps prevent recurrence.

► [Of the numerous forms of therapy which are sometimes of value in this often difficult therapeutic problem, we have not had any experience with such hot and colorful therapy as pure phenol and brilliant green. Our principal approaches are (1) avoidance of wet work, especially that involving exposure to alkaline cleansers, (2) topical therapy with steroid or vioform ointment in pyogenic paronychias and with mycostatin ointment in monilial paronychias, (3) superficial x-ray therapy and (4) oral antibiotics where indicated.—Eds.]

"Spontaneous Ulceration of Skin in Koreans was observed by John Van Duyn and Chang Suk Lee.[2] Of 16 cases 9 were ulcers of the lower leg and 7 were distributed haphazardly over the lower portion of the body. The exposed location of most of the ulcers and a history of scratching strongly suggest that trauma plays an etiologic role. The ulcer is characteristically shallow irregular 5-8 cm. in diameter with a shiny reddish, granulating base and a raised, thickened margin, usually following a serpiginous course (Fig. 4). Section shows a nonspecific granulomatous reaction with no evidence of leishmania spirochetal or mycotic diseases. Cultures from six ulcers showed coagulase positive Staphylococcus aureus one of which was mixed with Bacillus proteus. The bacteria seemed to be anaerobic.

Treatment was of three types. Removal of dressings and simple exposure to air brought about slow improvement. Complete excision of the ulcer with split grafting of the

(2) Plast. & Reconstruct. Surg. 16:303-311, October 1955.

to avoid crust formation on the mucosa of the lip. This preparation alone failed to improve the condition.

All symptoms subsided completely and did not recur. The treatment was well tolerated.

► [A welcome addition to the armamentarium for a condition that has remained a therapeutic problem. Combined therapy with x-ray and topical hydrocortisone also has proved effective in some cases.—Eds.]

Formaldehyde Treatment of Plantar Warts is according to R. B. Coles[9] painless and results are achieved slowly. In 242 patients (average age 13.1 years) the affected area of the foot was immersed in a 3% aqueous solution of formaldehyde for 10 minutes morning and evening. Yellow petrolatum was used interdigitally to prevent fissuring. Healing was spontaneous in 13 patients and no treatment was required. Of the other 229, 113 were cured by formaldehyde alone in an average of 6.6 weeks. In 60 more, formaldehyde treatment was reinforced by superficial desiccation of the surface of the pared warts with diathermy and the cure time averaged 9.4 weeks. No cases of formaldehyde contact dermatitis were found but in several patients painful cracks developed between the toes which were quickly corrected with the yellow soft paraffin "guard." A fresh bottle of formaldehyde solution was necessary every 10-14 days. The treatment was successful in 49.3% of the patients in less than seven weeks.

► [A 50% cure rate in a group of patients whose average age was 13.1 years probably could be achieved with a variety of forms of therapy for plantar warts. What is impressive is that probably half of the cases in this age group can be cured by conservative forms of therapy including suggestion treatment. The practitioner, however, is faced with the as yet unanswered question as to the particular cases which are susceptible to conservative treatment!—Eds.]

Chronic Perionychia: Etiology and Treatment are discussed by F. F. Hellier[1] (Gen'l Infirm., Leeds) whose study is limited to primary and isolated cases affecting one or more fingers in 100 patients. It is commonest in middle age and in women (94.6), particularly housewives and domestic servants. Redness and swelling or "bolstering" of the nail fold at the base, giving a drumstick appearance, is typical. The nail fold is separated from the nail instead of being adherent, is usually tender and may have associated lymphangitis and adenitis. Nails are often distorted, ridged or discolored. Candida fungi may be found on nail scrapings but it is uncertain

(9) T. St. John Hosp. Dermat. Soc., pp. 18-19, Autumn, 1955.
(1) Brit. M. J. 2:1358-1360, Dec. 3, 1955.

marked objective impro ement and decrease of symptoms and 28% showed moderate improvement. Of six with seborrheic dermatitis, five showed marked improvement Two of four patients with atopic dermatitis of the scalp showed moderate improvement. When the liquid was used on psoriatic lesions f glabrous skin results were in general unsatisfactory Few patients complained of excessive oiliness of the scalp itching and burning

It is concluded that P & S liquid is a valuable addition to management of psoriasis of the scalp because of its capacity to control the lesions without the disagreeable odor staining irritation or sensitization so common to many antipsoriatic measures.

► [A combination of seemingly innocuous agents which, while of course not cure, is indeed worth trial in the symptomatic management of psoriasis of the scalp.—Eds.]

New Effective Shampoo Treatment in Seborrhea Capitis. Seborrhea capitis, especially the dandruff or sicca type is believed to affect almost everyone, in some degree through most of adulthood Treatment should be simple ea ily applied, harmless and effective in clearing the scalp and skin f oiliness, scaling and crusting during the acute phase and preventing recurrence. The three main therapeutic actions desi ed ar reduction of excessive oiliness keratolytic action to remove keratotic blocking of the pores (peeling effect) and germicidal action to minimize secondary infection. These actions are possessed by a new lathering cream shampoo (Fostex cream) wh ch was studied clinically in 251 patients by Edmund F Finnerty[4] (Boston) Dandruff or seborrhea sicca was present in 173 The seborrhea capitis was generally severe and patients had had many and varied topical med ca tions before During the acute phase patients were treated w th topical medication to support the antiseborrheic shampoo When the acute phase subsided, all such med cation was topped Fostex cream was continued as sole treatment for control of the remaining symptoms and prevention of ecurrence

The a tiseborrheic shampoo dries the scalp and removes scales quickly Results were excellent in 208, good in 34 and f in 6 patients. Three showed excess e dryness from the

(4) New England J Med 253 4 4-6, Sept. 27 '954

denuded area, resulting in lost grafts due to undermining of pus (two patients) showed recurrence of the infection at the edges of the graft with a return of the raised margin (four patients) or healed rapidly with a minimum of infection (two patients) Those treated by application of chlortetracycline



Fig 4 —Typical pretibial ulcer showing shallow shiny base and irregular outline with raised margin This case was treated by excision of the ulcer and skin grafting (Courtesy of Van Duyn, J and Lee C. S Plast & Reconstruct. Surg 16 303-311 October 1955)

in saline 1 1000 with or without preliminary excision of the ulcer uniformly had the best result Intramuscular injection of penicillin did not seem to give beneficial effect

► [The fact that wet dressings with chlortetracycline effected the best therapeutic results is just another example of the value of appropriate external therapy —Eds.]

Modified Liquid Petrolatum Preparation Its Use in Management of Certain Common Dermatoses of the Scalp. Marion B Sulzberger and Jacobo Obadia[3] evaluated a relatively new preparation a mixture of less than 1% phenol liquid petrolatum and sodium chloride solution (P N S Liquid) The liquid was rubbed into the affected area every night for 2 20 weeks for an average of 6 weeks Improvement was judged by diminution or absence of erythema and scaling Subjective improvement was reported by the patient as relief from pruritus and scaling

Of 56 patients with *psoriasis of the scalp* 28 (50%) showed

(3) A.M.A. Arch. Dermat. 73 373-375 April, 1956.

cessive dryness burning and occasionally itching These undesirable effects of soaps on such skin are partly due to their alkalizing action in aqueous solution. Since soaps are salts of weakly ionized fatty acids and strongly ionized alkalis an alkaline solution always results on hydrolysis. This alkaline solution is well tolerated when soaps are used within reason on "normal" healthy skin, for the surface, by means of surface acids buffer systems and other homeostatic mechanisms, is able to maintain or recover its required acid pH of 3.5-6.0.

Frederick Swanson[a] (New York Univ Post-Grad. Med. School and Skin and Cancer Unit) tried a neutral detergent bar (Dove) which gives a lather of pH 7.0 on 200 selected dermatologic patients. Of these, 135 had dermatoses often intolerant and 26, dermatoses sometimes intolerant of common toilet soaps. No ill effects from regular use of the neutral detergent bar were seen in about 85% of patients with presumably generally poor tolerance for toilet soaps This greater tolerance for the neutral detergent bar is thought due to its neutral (pH 7.0) lather compared with the alkaline (pH 10.0) lather of most common toilet soaps

► [We have had extensive experience with this detergent bar and it is our impression that it is often better tolerated than are ordinary toilet soaps Since it is cosmetically highly acceptable it is more likely to be used consistently by soap-sensitive patients than the previously available bland nonalkaline cleansers —Eds]

Zinc Oxide A New Pink, Refractive Microform Crystal is described by Bernard Appel, Leslie M. Ohmart and Robert F Sterner Zinc oxide, one of the most used topical agents and some of its related materials, calamine and neocalamine, have been used for protection of the skin to add bulk to topical preparations, as an absorbent or adsorbent of secretions and for cosmetic purposes. An attempt was made to repeat the experiments of Haxthausen in which a bactericidal effect of zinc oxide was demonstrated, but no significant bactericidal or bacteriostatic action was shown on the common skin organisms tested. In this experiment, neo-zinc oxide hyperfin (Merck) replaced the standard zinc oxide preparations previously employed.

Neo-zinc oxide hyperfin is a new form of chemically pure zinc oxide. It is manufactured by a process of micronization

[a] J.A.M.A. 162: 39-41, Sept. 29, 1956.
[b] A.M.A. Arch. Dermat. 73: 316-324, April, 1956.

shampoo and it had to be discontinued. These were the only patients who failed to benefit

► [This preparation consists primarily of a combination of anionic surface-active agents (sodium lauryl sulfoacetate, sodium and alkyl poly ether sulfonate and sodium dioctyl sulfosuccinate) 2% micropulverized sulfur 2% salicylic acid and 1% hexachlorophene. In our experience also, it has proved to be a worthwhile addition to the medicated shampoos for seborrhea capitis as well as a drying cleanser for washing the face. For extremely mild cases of acne, as seen in early adolescent years, the cream alone is at times sufficient treatment when used with water as a face soap. —Eds.]

Selenium Sulfide in Treatment of Pityriasis Versicolor was tried by Harry M Robinson Jr and Stanley N Yaffe[5] (Univ of Maryland) on 32 patients aged 13-57 In all instances diagnosis was established by microscopic study of ink potassium hydroxide preparations A water miscible ointment base containing a 1% solution of selenium sulfide was dispensed in 1 oz tubes to the patients They were advised to take a shower with warm soapy water thoroughly rinsing the skin to remove all traces of the soap and then to pat the skin dry with a towel Towels and all clothing worn next to the skin were to be thoroughly laundered and dried before using them again After the bath a thin film of the ointment was to be lightly massaged into the involved areas twice daily The bath was to be repeated every three days. At the end of one week when the patients reported to the physician for further observation instructions were given to each to have some assistance at home in applying the medicament so that all of the areas would be treated The routine was repeated for a second week and then discontinued.

After one year no recurrence of the eruption was noted in 28 patients There was no discoloration of the treated area nor were any unpleasant subjective symptoms noted No adverse reactions were encountered

► [This treatment, as reported by the authors, yields a higher percentage of "cures," achieved in shorter period, than any other form of therapy known to us.

In view of the possible systemic toxic effects which have been feared following the percutaneous absorption of selenium sulfide, careful follow up of patients so treated must be carried out at least until much further experience has been accumulated.—Eds]

Clinical Evaluation of New Neutral Detergent Bar On skin that is abnormally dry sensitive or diseased common toilet soaps frequently cause irritation and a sensation of ex

(5) J.A.M.A. 162 113-114 Sept 8, 1956

2. ECZEMATOUS DERMATITIS
ATOPIC DERMATITIS AND URTICARIA ALLERGY

Contact Photodermatitis, according to Wiley Sams[9] (Miami, Fla.) is an altered skin reaction induced by application of various agents and following exposure to the sun. Among 290 patients seen in 20 years, lime oil was the cause of dermatitis and pigmentation in 186 and perfume and toilet water in another 43. Many patients develop dermatitis on exposure to the sun, limited to areas where sun-screening preparations have been used and appearing as eczematous papular or papulourticarial types.

Girl, 5 had a papular eruption on exposed parts after application of two sun-screening preparations and subsequent exposure to sun. After the reaction subsided, patch testing produced no reaction with either preparation, but later exposure to an erythema dose of ultraviolet light produced sensitivity reaction in an area covered by Neo-A-Fil cream. No further light sensitivity occurred after this subsided.

Experiments were performed to test the effect of various sun-screening substances on normal skin and on skin painted with light-sensitizing substances.

Experiment 1.—The right forearm was streaked with 1:100 alcohol solution of Shalimar perfume. Digalloyl trioleate 3.5% in alcohol, 5% menthyl anthranilate in alcohol, 1% aqueous chloroquine phosphate and 1% aqueous quinacrine were then applied across the streak. The arm was exposed for one hour to the noon sun. Shalimar had previously produced berlock dermatitis. Quinacrine and menthyl anthranilate blocked erythema from sun exposure. Chloroquine had no screening effect. The digalloyl trioleate site and the Shalimar streak showed sensitivity reactions.

Experiment 2.—The axilla was streaked with a solution of digalloyl trioleate and Neo-A-Fil and exposed to sun for one hour. First degree erythema developed in the unstreaked, but not in the streaked sites. However after 36 hours, itching developed in the streaked areas and papulourticarial eruption appeared. Control sites not exposed to sun showed no reaction.

Experiment 3.—Experiment 2 was repeated, using only 3.5% alcoholic solution of digalloyl trioleate and exposure to sun for one hour. Erythema was less pronounced, but papular dermatitis at the border of the streak appeared after 27 hours.

Experiment 4.—Experiment 3 was repeated and erythema produced on the unstreaked area with cold quartz lamp. The prep-

9) A.M.A. Arch. Dermat. 73:142-148, February 1956.

of standard zinc oxide By change in molecular structure its crystal lattice reflects light so that its color is moderate orange-pink ("flesh) The particulate size is small, about 200 Å Particle aggregates can be milled to as small as 1 µ. The prepared powder has a characteristic mobility and is easily dispersed when rubbed on the skin to which it adheres with a dry palpable tenacity It combines pharmaceutically as easily as white zinc oxide and is cosmetically effective. It may replace white zinc oxide and calamine in topical dermatotherapy

Therapeutic Experiences with Trypsin in Dermatology and Venereology V G Rinaldi[8] studied the proteolytic effect of trypsin as an adjuvant to penicillin in 80 patients with varicose ulcers ulcerated basal cell epitheliomas primary multiple cutaneous gangrene bedsores bullous streptococcic infections nonspecific chronic urethritis and specific and nonspecific cervicitis Triptocillina a mixture of 1,000 units of trypsin and 100 000 units of penicillin G in a lyophilic state dissolved at time of use in the sterile solvent sold with the preparation was applied locally every day for varying periods as gauze compresses or vaginal tampons or was instilled into the urethra or injected into the cervical canal

Tolerance was always excellent even when 4-5 cc. was injected into the cervical canal to remove mucopurulent secretions Results were excellent in chronic varicose ulcer and bullous streptococcic infections with removal of the pseudomembranes and exudate and restoration of granulation They were good in chronic nonspecific and acute and subacute specific cervicitis In these conditions better results could be obtained if the time of contact for lytic action with the impaired tissue could be prolonged Ulcerated epitheliomas and primary multiple cutaneous gangrene were not benefited. Results were difficult to evaluate in nonspecific urethritis because of its subacute or chronic course with scarce mucopurulent secretion and desquamating keratotic epithelial cells The exudative phenomena and the microbial flora were, however markedly diminished

► [The principle of first removing debris, crusts or scales from surfaces of lesions to be treated by local medicaments is an important one Thus, the superficial crust in impetigo should be soaked or washed off before application of antibiotic ointments, the scales of psoriasis should be softened and removed before applying antipsoriatic measures, etc., etc —Eds.]

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(8) Minerva dermat. 31 126-128, April, 1956.

one week, and in a few it was about three weeks. The hands forearms, or both were affected. In only one patient the arms and the extensors of the forearms were involved, and in another the face, especially the upper eyelids. The dermatitis was subacute or acute, with variable degrees of redness, edema and invariably many vesicles. The eruption on the hands comprised redness with vesicular outbreak on the fingers, dorsa of the hands and, at times on the thenar eminence. The eruption on the fingers resembled acute tinea. In only one patient were the palms affected, the eruption being confined to the base of the fingers. Patients who wore gloves had only involvement of the forearms.

Three patients with sensitization dermatitis were not engaged on the trimming job. One, a woman, sorted wet carrots with ungloved hands. After 18 days, a dermatitis appeared on the hands and lower forearms. The second patient handled uncut, unpeeled wet carrots. His hands and forearms were constantly wet. After 16 days, a dermatitis appeared on the hands, forearms and face. The third patient removed with ungloved hands peeled wet carrots. After 15 days, a dermatitis appeared on the hands and lower forearms. Apparently the sensitizing principle of carrots is water soluble.

The dermatitis disappeared in one to two weeks after the worker's transfer from the trimming job and cessation of exposure and recurred when this work was resumed. With one exception, the patients were new employees not exposed to carrots in any previous work.

Patch tests were performed with the surface of an unpeeled raw carrot and also with the surface of a slice of the same carrot. The tests were read in 24 hours. All patients reacted positively to all tests. The authors never observed continuation of carrot dermatitis or its recurrence through cross-sensitization.

The edible umbellifers—carrots, parsnips, parsley, celery (including celery salt) and turnip-rooted celery—should be considered as a cause of dermatitis of the hands in housewives. It is likely that exposure to these vegetables is not sufficient in degree or duration to cause sensitization. This may not apply to kitchen and restaurant workers and to employees constantly making salads in which these raw vegetables are handled.

► (This article is well worth reading in the original, since it contains

aration protected against erythema, but no sensitivity reaction was obtained.

These experiments indicate that the sun screening agent protects skin from sunburn but sensitizes it to ultraviolet light of longer wavelength Differences in reaction may be based on an acquired altered state of skin reactivity in those who develop the papulourticarial response. Attempts to demonstrate passive transfer of this type of sensitivity by usual methods using both Shalimar perfume and digalloyl trioleate solution were unsuccessful It may be that this is an allergic reaction despite negative passive transfer The antigen may be a photosensitive complex of epidermal protein and hapten in this case the chemical used and the delayed papular reaction may be triggered by exposure to sun

► [Sams excellent report indicates the extent of the problem of photosensitivity Two hundred and ninety pertinent cases were seen by this author alone over 20 years. Further progress in this highly important area of hypersensitivity can be expected from the use of improved experimental technics, including the use of artificial sources of light such as, for example monochromators.

The technics used in these tests do not clearly prove that it must be wavelengths longer than the sunburn spectrum which caused photodermatitis of the skin sites to which digalloyl trioleate was applied. It appears possible also that the photodermatitis due to the sunscreening agent might have been produced by wavelengths in the sunburn spectrum. These wavelengths, even though reduced in quantity by the digalloyl trioleate at the skin surface to a point where they do not cause visible erythema might be assumed to penetrate into the sensitized skin in sufficient quantity to elicit a photoallergic response —Eds.]

Sensitization Dermatitis to Carrots Report of Cross Sensitization Phenomenon and Remarks on Phytophotodermatitis. In their experience with employees processing a variety of vegetables Joseph V Klauder and John M Kimmich[1] found carrots an outstanding cause of sensitization dermatitis They report an outbreak involving 13 employees.

In the trimming process employees handle mechanically peeled, wet but otherwise untreated, raw carrot The wet carrot is held in the left hand and with a knife in the right hand the ends are cut off fragments of peeling may be removed and the carrot is then sliced When this work is done sitting the forearms rest on a stainless steel topped table wet with carrot juice and water There is no such table contact when the work is performed standing The incubation period of the dermatitis was usually about two weeks after working on the trimming job In only one patient was it as hort as

(1) A.M.A. Arch. Dermat. 74 149-158, August, 1956.

ible light) and (3) over 700 mμ (infra red rays) The reaction usually develops rapidly after ½ 1 minute s exposure and usually disappears within 1 hour without leaving erythema or pigmentation. Blum attributes redness and swelling to an H-s bstance, corresponding to the triple response of Lewis and the histamine reaction of Wucherpfennig

Man, 25 for four years had typical solar urticaria whenever he was exposed to the sun. The urticaria usually disappeared in an hour and was more severe on parts of the body ordinarily covered with clothing Window glass inhibited the reaction. H had had no previous urticaria except for severe reaction to insect bites. He appeared healthy but somewhat nervous, perspired freely had mild hand tremor and exophthalmos, with slight thyroid enlargement, and showed marked dermographism. Blood and urine tests (including urinary porphyrin) were negati e. H had been treated for long time with antihistamines and then with atraquine, without noticeable effect.

Experimental exposure of two areas on the back (one covered th glass 1 mm. thick) to irradiation with a Philips lamp at 1 m. produced an urticarial reaction on the uncovered patch within 15 seconds and on the glass-covered patch after about 30 seconds. Reactions were of similar severity and duration. With 10 seconds of irradiation, reaction sufficient to be called urticaria developed. By application of 10% para-aminobenzoic acid in petrolatum before radiation, the reaction could be reduced considerably The reaction as inhibited or absent areas where urticaria had developed shortly before W velength producing th reaction were determined by Rottier quartz spectroscope to be 313 and 334 mμ. These wavelengths also produced delayed reaction through glass.

Passive transfer of serum from th patient to five normal subjects (0 cc intracutaneously) followed in 24 hours by radiation, produced an urticarial reaction in all w thin 2 3 minutes. Reactions to radiation were still positi e after week, but tw weeks later urticaria failed to develop Irradiation of areas in which normal serum had been injected in these same test subjects showed no urticarial reaction

Treatment of the patient with phenergan* did not inhibit the urticaria, but cortisone decreased it. While still taking cortisone, 25 mg/day the patient was irradiated with increasing doses of ultra iolet light to produce desensitization This was difficult because of the extreme hypersensitivity I the early tages of treatment, he could tolerate no more than five seconds of irradiation without reaction, but gradually he could take longer exposures. Treatment was continued into the second year The favorable result w probably due to thickening of the stratum corneum rather than to true immunization

Urticaria Following Exposure to Ammonia Fumes. George F Morris (Boston) reports the occurrence of h ves in two

M A Arch Indust, Health 11-400, May 1956.

wealth of useful and interesting information. Apparently handling of carrots by housewives rarely produces allergic eczematous contact dermatitis since the exposure is likely to be slight and transitory Moreover ingestion of carrots and related products apparently failed to produce flare-ups of the hands even in workers highly sensitive to carrots, a very important fact.—Eds.]

Acetic Acid Sensitivity as Cause of Cold Urticaria is described as a specific etiologic factor in one patient by Richard D Wiseman and Daniel K Adler[2] (Syracuse N Y)

Man, 35 had a four year history of recurrent hives on exposed parts of the body after exposure to cold. He also showed swelling of the throat following ingestion of ice cream or very cold drinks He did not have hives while swimming in the summer Urticarial lesions formed three to five minutes after application of an ice cube to the skin. Passive transfer tests with five week old serum showed no response to ice cube tests. After elimination of sauerkraut and dill pickles from the diet, the cold urticarial response could no longer be elicited. When these foods were added to the diet, the reactions again could be produced. He showed no unusual reaction to ingestion of ice cream after a placebo mixture but developed marked pharyngeal edema when 2 ml. of 2% acetic acid was added. When 0 1% citric, lactic and acetic acids were injected intradermally an urticarial response was produced by ice cubes over the acetic acid site.

It is concluded that the patient had a specific chemical sensitivity which produced cold urticaria. Following elimination of the chemical from the diet the allergic activity quickly subsided Acetic acid may have acted as a hapten to form a complex antigen or the cold may have been a catalyst in the allergic reaction The new technic presented may be valuable in the study of patients with physical allergies due to chemical sensitivities

► [A very interesting revelation which vividly points out the unusual and unsuspected combination of factors which may be necessary to cause allergic skin lesions and the methods which may be necessary to demonstrate such unusual sensitivities (in this case combined testing with the chemical and physical agent) In principle this form of cold allergy is not unlike the type of photoallergy, first described by S. Epstein, which requires the presence of a chemical, e.g. sulfanilamide, and exposure to the proper source of light.—Eds]

Urticaria Solaris according to F P Scott[3] (Univ of Amsterdam) is a rare form of physical urticaria caused by the sun's rays, first described in 1905 It appears that the total spectrum may be divided into three groups that produce distinctly different urticarial reactions by wavelengths (1) shorter than 370 mμ (ultraviolet) (2) of 370-700 mμ (vis

(2) J Allergy 27 58-56, January 1956.
(3) Nederl. tijdschr geneesk. 99 3879-3886, Dec 24 1955.

sible for urticarial lesions and this is strongly supported by observations made with antihistamines and a histamine liberator Antihistamines can suppress or mitigate urticaria when given systemically or locally Since the urticaria in the author s observations was in ariably associated with sweat ing it may be supposed that the intermediate step which links acetylcholine with histamine is connected with sweat gla d acti ity Sweat itself may act as a histamine liberator in these patients or some substance formed during sweat gland metabolism may be the intermediary

Cholinesterase Levels in the Skin in Cholinogenic Urticaria and Pruritus. I A. Magnus and R. H. S. Thompson[6] (Guy s Hosp Med. School London) infer that the mech anism of whealing and tching n cholinogenic urticaria and pruritus, if brought about by release of acetylcholine at nerve endings as postulated by Grant *et al* may poss bly be due to reduced ctivity of cholinesterase. Results of investiga tions seem to upport this conjecture Test f r cholinesterase and pseudocholinesterase in biopsy specimens of skin from 5 patients with cholinogenic urticaria, 2 with cholinogenic pruritus and 23 with different, noncholinogenic whealing were studied. Cholinesterase and pseudocholinesterase ac tivity was estimated, and intradermal tests with acetylcholine were carried out. In all seven patients with cholinogenic urticaria and prur tus, the level of pseudocholinesterase was low On the basis of ailable evidence it is not possible to state in what structure of the skin the reduced cholinesterase acti ity lies, but the sympathetic nerve system seem to be the pathway of the nervous mechanism. Results of intra dermal test with acetylcholine were inconclusi e. The serum cholinesterase lev l determined n four male patients with cholinogenic urticaria and two with chol nogenic pruritus, w within normal range

► [More cases of cholinogenic urticaria and itching will have to be studied (as this way) for cholinesterase levels before definite conclusions can be drawn The results of Magnus and Thompson, however, suggest that whealing and itching in these cases might ell be due to reduced cholinesterase activity rather than to true allergic hypersensitivity —Eds.]

Wasp Venom Allergy and Immunity Cl n cal imm ity to h menoptera (wasps, bees, ants etc.) has been achieved in few person by injection of graduated amou ts of whole body extract a well a by accidental or planned intermittent

[6] Brit J Dermat 68 283 289 September 56

workers after six different exposures to the fumes of ammonia a simple nonorganic chemical

CASE 1.—Man, 28, had been exposed to strong ammonia water for 12 14 hours after which he broke out with what he termed whelks. Five weeks later after a similar exposure the eruption again appeared. Cortisone was administered, but subsequent exposure to ammonia produced a third recurrence.

CASE 2.—Man 31 broke out with wheals similar to those in Case 1 after a similar exposure. The wheals disappeared when he stayed away from work, but recurred when he returned. He also broke out while riding in an automobile with men who had been exposed to ammonia fumes. Examination revealed multiple urticarial lesions on the trunk, arms, face and neck.

► [This report of urticarial sensitivity to ammonia causes one to wonder whether diaper dermatitis, ascribed to the alkalinizing effect of the urea in urine could not, in some cases, be due to an allergic contact sensitivity to the ammonia which is liberated.

In urticaria due to inhalant substances, the etiologic factor is found but rarely probably because of the technical difficulties involved. Among other examples of urticaria due to gaseous materials were those reported by Pirila (Acta allergol. 7.397 1954) who described one case each of urticaria and contact dermatitis due to gaseous sulfur compounds and by Rappaport and H ffman (J.A.M.A. 116.2656, 1941) who described in detail the chemical aspects of the sensitivity in a patient with urticaria due to formaldehyde, tobacco smoke and certain fried and broiled foods.—Eds]

Nervous Pathway Mediating Cholinogenic Urticaria. Cholinogenic urticaria is provoked through stimulating efferent nerves by emotion exercise or warming the body Andrew Herxheimer[3] (St Thomas s Hosp Med School London) observed in three patients with cholinogenic urticaria that the cholinergic fibers responsible belonged to the sympathetic nervous system Unilateral cervical sympathetic procaine block prevented induced urticaria on the blocked side General sympathetic block with hexamethonium almost completely prevented urticaria. Axon reflex sweating elicited by various local stimuli in these patients was followed by satellite wheals around the point of stimulation Whealing also occurred on the face and neck after gustatory sweating induced by chilies

Local stimuli which reproduced the typical urticarial lesions invariably caused sweating and vasodilatation Thus, there was no evidence for the existence of separate vasodilator fibers to the skin.

Intermediate steps between liberation of acetylcholine at nerve endings in the skin and appearance of urticaria are not known Lewis gave much evidence that histamine is respon

(3) Clin. Sc. 15 195-205 May 1956.

Wasp venom appears highly satisfactory for immunization against wasp sting reactions as judged by several criteria, including deliberate and accidental stings. However the exact identity of the offending wasp or bee must be learned since immunization with another type might provide protection against the common allergen, but not against the type-specific variety Although this risk might be avoided by using a mixture of the several hymenoptera venoms, this carries the theoretical danger of induced sensitization for the etiologic varieties Since venom hypersensitivity seems a more or less normal response of man to parenteral introduction of foreign protein and has many resemblances to serum disease, drug idiosyncrasy and experimental anaphylaxis it seems essential to avoid parenteral use of venom whenever possible

A few as six venom sacs appeared sufficient for protection and could be administered during a single, prolonged visit without untoward effect.

► [The development of material free from contaminants to be used for hyposensitization in cases of severe sensitivity to the stings of hymenoptera is a real step forward. The finding of group specific and species specific allergenic components in material from hymenoptera is not unexpected in view of similar findings with fungi, foods (e g molluscs) etc. —Eds.]

Bullous Dermatitis of Feet Caused by Pure Nylon was observed by M N Prassas[4] (Athens)

Man, 50, had had dermatosis for one week, involving the distal parts of both feet, which appeared first as disseminated lesions on soles, heels and toes later the lesions became multiple bullae which made walking difficult. Because of hyperhidrosis pedum, he had bought and worn Nylon stockings on the day before onset of the eruption The plantar surfaces of both feet revealed bullous dermatitis, with size of bullae varying up to that of a large almond in the instep, few red papules were seen. Interdigital scaliness and itching were absent the rest of the body skin surface and the mucous membranes were clear Results of mycotic examinations were negative.

Patch tests with (1) water in which a piece of Nylon stocking had been boiled, (2) water in which piece had been kept for 24 hours and (3) alcohol in which piece remained for 24 hours, were negative When these pieces of Nylon were rubbed on the arm, local and distant reaction on the legs and around the navel appeared T exclude dyes and the stocking finish as possible causative factors, patch tests were made with undyed white and raw Nylon

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[4] Bull Soc franç de syph. 61 368-369, Nov-Dec 1953.

stings of live insects To limit the number of components in the immunizing material at the same time controlling the volume administered, Mary Hewitt Loveless and William R Fackler[7] (Cornell Univ) introduced the use of wasp venom (free from other body constituents and adhering contaminants such as pollen) The unit of antigen was temporarily the surgically removed venom sac. Response levels of normal young adults to venom of the yellow jacket wasp were delineated by concurrent tests of the skin and eye and a three minute sting with a live worker insect

Comparable tests of tissues of wasp-allergic subjects showed that lower venom concentrations sufficed for threshold response After immunization with yellow jacket venom however intracutaneous and conjunctival reactions of the patients approached those of the normal controls. Responses of immunized patients to deliberate insect stings also resembled those of the controls

Direct tests of sensitized persons and experiments with their serum in normal skin indicated that five of the hymenoptera (yellow jacket bald faced hornet paper wasp, honeybee and bumblebee) possess a common allergenic specificity while each also contains in its venom a component peculiar to it The honeybee appeared more closely related to the three wasps examined than was the bumblebee and the three wasps had much in common Each venom is probably a complex antigenic mixture

Three anaphylactic syndromes during early trials with venom immunization resembled the acute hypotensive reactions to histamine as was seen in the following patient.

Man had headache and flushing 10 minutes after completion of the day's course of 2.25 sacs of yellow jacket queen venom. He shortly had tachycardia, pounding in the head and chest and generalized heat and throbbing in the skin. The nasal passages became congested and he became apprehensive and felt cold in a warm room. Pulse rate rose to 160 and for a moment diastolic blood pressure could not be obtained. The face was mildly cyanotic. Intramuscular injection of 0.25 ml. 1 1000 epinephrine promptly relieved all symptoms except an intense headache, which yielded gradually to aspirin. Two mild reactions of this type followed injections on the next two days pulse rate rose while systolic and diastolic pressures fell moderately for a few minutes. Three months later 6.4 sacs of the same antigen in four hours were tolerated without subjective or objective evidence of allergy

(7) Am Allergy 14:347 366, Sept.-Oct., 1956.

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1) Bull. Soc. franç. de syph. 62 [illegible] Nov.-Dec., 1955.

material Positive results of both tests confirmed that the Nylon itself was the sensitizing agent

► [To our knowledge this is the first reported instance of allergic eczematous contact dermatitis due to Nylon material itself. A very great number of items are made from Nylon in these times, among them clothing, sutures, fishing line, rope gears, glasses frames, curtains and rugs. All previous cases have been shown to be the result of the dye sizing or other chemical added to the Nylon fiber during the manufacturing processes Of course, if Prassas finding is correct, it still does not alter the fact that Nylon fiber itself has an extraordinarily low sensitizing capacity—Ed]

Nylon Stocking Dermatitis commonly affects the dorsa of the feet and toes backs of the knees and inner part of the upper thighs according to C D Calnan and H T H Wilson[9] (London) The eruption may also involve the heels, soles and plantar surfaces of toes is usually symmetrical and may be acutely vesicular and exudative or dry and scaly Six cases are reported in women aged 25 50 with characteristic manifestations and sensitivity reaction proved by patch testing

Nylon stocking dermatitis results from sensitivity to the dye usually an azo variety Yellow dye produced a reaction in five of the six women the black dye produced the reaction in the sixth There was no cross sensitivity to procaine, sulfanilamide liquor azorubri benzocaine and paraphenylenediamine except to the latter in one patient No sensitivity has been reported to anthraquinone dyes and there was no cross sensitivity in the six patients reported It is suggested that dyes derived from this chemical be used A logwood dye has been used for black Nylon stockings and no reaction to it has been found in patients with dermatitis from other black Nylon

► [While by no means a new finding according to the author it is the first such report from England. The incidence of allergic contact dermatitis due to azodyes in Nylon stockings in the United States is now apparently much less than when the first report was published by S. Dobkevitch Morrill and the senior editor in 1947 In our experience a minority of patients with this type of dermatitis have their eruption over most or all the skin area exposed to the stocking The majority show lesions principally on the dorsa of the feet and in the popliteal spaces. The involvement on the inner aspect of the thighs has not been especially noted in our patient material—Eds.]

Contact Dermatitis Due to Acrylic Materials Used in Artificial Nails was observed by Orlando Canizares[1] (New York)

Woman, 29 manicurist, about six months before observation received instructions on the application of artificial plastic nails,

(9) Brit M J 1 147 149 Jan 21 1956
(1) A.M.A. Arch. Dermat. 7 141 143 August, 1956.

procedure which consists of applying with a small brush a mixture of liquid and a powder to the nail of the customer The operator places crescent-shaped cardboard round the tip of the finger and, after wetting the brush in the liquid, picks up some powder and applies it to the nail. The liquid is constantly applied to keep the material in the desired shape. With successive applications, nail of the desired length is built and the cardboard removed. The artificial nail may be filed and covered with nail polish. During the operation, the mixture or liquid often comes in contact with the operator's fingers while she holds the customer's finger

After applying these artificial nails for about three weeks, the manicurist noted dryness and scaliness of the tip of the left thumb and middle finger and, to less degree, of the index finger The eruption became gradually worse. When seen, she had dermatitis localized to the left upper extremity involving the hand, wrist and forearm. The thumb and middle finger were most severely affected. They presented an eczematous dermatitis. Diffuse erythema and slight edema of the ulnar side of the left wrist and forearm were also present.

The patient continued to work with the acrylic materials but was advised to use protection to avoid contact with the irritating substances. A thin layer of tin-foil paper was wrapped around the fingers and rubber gloves were used. Despite these precautions, the eruption became more severe, and she was instructed to stop orking With soothing topical applications and superficial grenz ray therapy the eruption improved.

Repeated contact with acrylic materials, especially with the sen tizing liquid monomer is known to be responsible for contact dermatitis in dentists and dental technicians. Artificial na ls made with these materials will undoubtedly increase the number of such eactions Application of toe nails mad of acrylic substances has been used by podiatrists in the treatment of tinea ungu um. No instance of sensitization has been reported.

► [With the increasing use of acrylic materials, it can be expected that dermatitis due to the monomer will be seen with greater frequency and in greater ariety of locations. W have seen acute paronychias (without eczematous involvement) of several fingers on one patient following the use of plastic nails to cover the deformed and partially disintegrated natural nails and the irregularly roughened nail bed When these acrylic nails ere discontinued, the paronychias immediately improved. A patch test applied to the patient' back with nail" prepared according to the manufacturers' direction was strongly positive.—Ed.]

Allergic Hypersensitivity to Antiseptic Soap, contain ng tetramethylth uram disulfide to reduce th bacterial popula tion of th urface and thu control axillary odor is discussed by Irv H Blank[2] (Harvard Med. School) The antiseptic is the same chemical as that used a an ccelerator in the

2) J.A.M.A. 60 1225 1226, Apr 7 1956.

material. Positive results of both tests confirmed that the Nylon itself was the sensitizing agent.

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(9) Brit. M. J. 1:147-149, Jan. 21, 1956.
(1) A.M.A. Arch. Derm. 74:141-143, August, 1956.

balt. All but two chromate sensitive patients had positive reactions to both patch and intradermal tests.

Clinically the delayed intradermal reaction varied from papular to eczematous, a reaction being considered positive when a papul larger than 5 mm. was present for at least 48 hours Histologically too the picture varied. The corium showed edema and a spotty yet dense, perivascular infil trate consisting mainly of lymphocytes. The ep dermis was usually normal. A biopsy section from the site of a patch test with potassium dichromate showed a thickened and edematous epidermis and several intraepidermal spongiotic vesicles which had been shed in the form of crusts and were practically all periporal. The corium showed pronounced superficial edema with accumulations of eosinophils and perivascular lymphocytic infiltrates The intradermal test has been interp eted as presenting a purely vascular and perivascular reaction except for changes in the epithelium of hair follicles in the patch test, the sweat pores appear to ha e acted as ports of entrance for the chemical, with acute edema of the epidermis resulting and widespread vascular and perivascular reactions as in the intradermal test. Present ev dence indicates that eczematous- and tuberculin type sensitivities are immunologically identical, except for the shock organ

The concept of localized sensit ty must be re-evaluated. E en in the presence of generalized sens ti ty increased local sensiti ty at the primary site of contact often exists, which may expla n why a contact dermatitis from nickel somet mes occurs only on certain sites of contact with the causative chemical e g dermatitis from nickel-containing garters may occur only on one leg Nickel contact dermatitis presents some li ical peculiarities t usually is a papular or papulo esicula rather than a bullous dermatitis It may produce prurigo-l ke papules or lichenified lesions resembling atopic dermat t Meta tatic eczema may occur at d sta t tes or the eruption may spread for some distance be ond the ea of direct contact with a metal object uch as ring (Fig 5) Nickel contact dermatitis commonly occurs patient with topic dermatitis Of 34 patients with nickel sen t ty 10 howed gns of atopi dermatitis as well. The lation hip between the two is not known

rubber industry and in rubber adhesives in shoes. Patients shown to be allergic to the chemical in rubber adhesives were tested for sensitivity to the soap and to the specific chemical. The soap in 8% aqueous solution was applied to the skin and an identical soap without the antiseptic was used as a control. The antiseptic and a rubber accelerator were tested in 1% concentration in petrolatum. Test samples remained on the skin for 48 hours. Results of the tests on six patients were: all who showed a vesicular reaction to the rubber accelerator reacted similarly to the antiseptic, to the antiseptic soap and to an 8% solution of the soap. Reactions to the control soap and the 8% solution of control soap were insignificant. One patient allergic to a chemically related rubber accelerator did not react to the antiseptic or the antiseptic soap.

Although it has been suggested that, in persons not previously allergic to the compound in the antiseptic, a hypersensitivity to it might develop from repeated use of the soap, clinical trial has shown this to be unlikely. No rising trend in incidence of allergy to the new product is apparent. However, development of dermatitis from the use of this soap is possible.

► [In our continued experience with the use of a soap which contains tetramethylthiuramdisulfide, we have not encountered any instances of allergic sensitization to this antiseptic. For further comment see the leading article this YEAR BOOK (p. 22).—Eds.]

Contact Dermatitis Due to Nickel and Chromate: Observations on Dermal Delayed (Tuberculin Type) Sensitivity. Stephan Epstein[3] (Univ. of Minnesota) observes that dermal delayed sensitivity (tuberculin type) plays a far more important role in contact dermatitis from nickel and chromates than has been assumed heretofore. In 34 patients with nickel sensitivity, patch tests with 10% nickel sulfate solution and intradermal tests with 0.02-0.05 cc. of a 1:40,000 dilution of nickel sulfate were made. Most patients reacted to both tests, the patches producing eczematous or papular reactions, and the intradermal tests, tuberculin type papular reactions or a vesiculopapular dermatitis. Of the tested patients, 42% also had a positive reaction to copper, but usually less severe than to nickel. Three of 31 nickel-sensitive patients reacted to potassium dichromate and 5 of 11 patients reacted to co-

(3) A.M.A. Arch. Dermat. 73:336-355, March, 1956.

► [A thought-provoking article which is "must" reading for those interested in dermatologic immunology. It would appear that dermal sensitivity to metals, as demonstrated by positive *tuberculin type* responses, is not adequate to explain all instances of strictly localized allergic eczematous sensitivity or localized areas of much greater sensitivity than the rest of the skin (see leading article). For example, it would be hard to explain on this basis those cases in which certain skin sites regularly flare up on adequate exposure of distant sites to the responsible allergen.

In a series of at least 100 nickel-sensitive patients tested by A. A. Fisher and collaborators at the New York Skin and Cancer Unit only three instances of cross-sensitization between nickel and cobalt have been found. The cases of cobalt sensitivity did not cross-react with nickel.—Eds.]

Allergic Eczematous Contact Dermatitis Due to Metallic Nickel. Alexander A. Fisher and Alfred Shapiro (New York Univ. Post-Grad. Med. School and Skin and Cancer Unit) found nickel to be the cause of dermatitis in 198 patients seen over five years. Such patients invariably reacted positively to patch tests with 10% nickel sulfate solution, and the only chemical that surpassed nickel as the causative agent of such strongly positive reactions was paraphenylenediamine. The optimal concentration for patch testing is 5%.

The commonest locations were the ear lobes (from ear rings), thighs (from garter clasps and metal chairs), hands and wrists. Patients have successfully used various methods of covering nickel objects or avoiding contact with them. Forty who were sensitive to nickel were retested 2-17 years after their original clinic attendance for nickel dermatitis: 90% retained their sensitivity to nickel, including patients with follow-up periods as long as 17 years, and 10% had lost their sensitivity during a follow-up of 2-5 years. Continued exposure or no apparent exposure to nickel appeared not to affect persistence of sensitivity. No cross reactions to potassium dichromate or copper sulfate were noted, but two patients also reacted to cobalt.

Nickel Dermatitis was studied by C. D. Calnan[5] (St. John's Hosp., London) in 400 women. Over 95% of them had stocking suspender dermatitis as the first manifestation of nickel sensitivity. In only 19 did the dermatitis begin elsewhere, the commonest site being the ear lobes (from ear rings). Trauma and friction alone are exceptional as a cause of dermatitis.

Nickel dermatitis appears as a primary eruption on direct

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(4) J.A.M.A. 1[illegible]: 712-721, June 23, 1956.
(5) Brit. J. Dermat. 68: 229-234, July-Aug., 1956.

Three patients with chromate sensitivity showed allergic sensitivity to soap although chromates are not used in the manufacture of soap Chromate dermatitis is a chronic and resistant process persisting long after contact with chromates has been eliminated. In some instances infectious eczemas are superimposed in others, the classic signs of atopic dermatitis seem to develop Persons with a severe dermal type of sensitivity present a variety of clinical forms of eczema

It is possible that with proper dilutions intradermal testing with simple chemicals is no more risky than patch test



Fig 5 Metastatic nickel eczema on finger spreading beyond contact with ring and other fingers (Courtesy of Epstein, S. A.M.A. Arch. Dermat. 73:236-253, March, 1956.)

ing If dermal sensitivity has a significant role in contact dermatitis desensitization could be tried as a therapeutic procedure, although with nickel sensitive patients, elimination of the contact is simpler and easier Some favorable results in preventing nickel dermatitis have been reported with chelating agents, such as edathamil disodium if the ointment is applied frequently

The recognition of dermal delayed sensitivity in contact dermatitis is of more theoretical than practical interest. It appears that the skin has a double allergic coat one in the epidermis and another in the corium In contact dermatitis either or both may be affected Dermal sensitivity may explain the prolonged course in certain cases of contact dermatitis from metals, and also features of localized dermatitis and the phenomenon of localized sensitivity

tion in Formalin and sectioning will produce no alteration of distribution. Sections will then show nickel held in scales on the surface of the horny layer only penetrating deeper into the ends of the sweat ducts, and sometimes down the hair follicle lining

Attention has been called to the high incidence of eczema of the hands of women who have become sensitized to nickel through their stocking suspenders. It is unlikely that the eczema was caused by nickel in detergents since no measurable amount of nickel was found in them. Sweat may mobilize nickel, and a coin may elicit nickel sensitivity after a short contact b t it is not known whether this causes diffuse hand eczema. In most instances the hand involvement is probably a response to nonspecific irritants in women made more prone to eczema by their sensitivity to nickel.

For nickel-sensitive patients the use of Nylon suspender buckles is suggested.

[The reported higher incidence of hand eczema in women allergic to nickel may be accounted for by the possible effects of detergents in enhancing the reaction-producing capacity of potential allergens, in particular nickel. See abstract and editorial note to article of Kvorning and Svendsen (this Year Book) and of Nilzén and Wikström (this Year Book). Many of the garments worn by the fairer sex have some nickel attached, g clips, catches, zippers, hooks, snaps, buckles, etc., and these objects, as ell as many others containing nickel, are undoubtedly contacted daily.

The localization of the nickel around the sweat duct orifices as demonstrated by Wells is not unexpected if one considers the parakeratotic plug hich occludes the opening of the sweat duct and accounts for the pustule sometimes formed during patch tests with nickel sulfate.—Eds.]

Sensitization to Facial Tissues with Urea Formaldehyde Resin uggested as a possible etiologic factor in eyelid or circumoral dermatitis by Samuel M. Peck and Lawrence L. Palitz (New York). Both melamine formaldehyde and urea formaldehyde thermosetting resins, can condition paper to be strong when wet. Often, the incompletely cured resins cause dermatitis. Formaldehyde, particularly is a highly sensitizing substance.

Method.—Facial tissue A had no additi B had added wet strength, urea-formaldehyde resin. Because of the low concentration of formaldehyde, the Draize-Shelanski repeated insult test was used. A patch was applied to the skin for 24 hours, then removed, and the skin was left free for 24 hours. The cycle was repeated 15 times. Fifteen males and 35 females were patch tested on the upper outer arm, the right was used for tissue B and the left for tissue A. A usage test was made daily for 30 days by rubbing tissue

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metal-contact sites and as a secondary eruption or areas of spread apart from such sites. The commonest secondary sites are elbow flexures eyelids sides of neck and face inner thighs and sometimes generalized. The secondary eruption behaves like a hematogenous spread similar to the id phenomenon in ringworm and other infections it is usually *symmetrical* Many patients had other varieties of eczema in addition to nickel sensitivity pattern Nickel sensitivity can be confirmed by patch tests with 1% or 2.5% nickel sulfate solution

The natural history of this type of nickel dermatitis varies. Patients with only primary eruptions recover easily when the metal contacts are removed. Once secondary spread has occurred the prognosis is not as good Treated on an out patient basis the eruption may not clear for many weeks or months recurrences often develop A notable feature is relapse of the secondary eruption without activity at primary sites

► [If nickel can produce secondary eruptions at sites distant from areas of direct exposure, it may be assumed that other metals as well as nonmetallic allergens could do likewise. The potential importance of this phenomenon may be gleaned from Calnan's observation that secondary eruptions occurred in three of every four cases of nickel dermatitis.—Ed.]

Effects of Nickel on the Skin. G C Wells[6] (Univ of London) observes that the commonest cause of specific allergic contact dermatitis in women in England is nickel. The sensitivity has usually been induced at the stocking suspender sites.

If a section of skin is soaked in a dilute solution of a nickel salt and then rinsed some nickel remains in the tissue and can be seen under the microscope if a suitable color reagent for nickel such as dimethylglyoxime and dithio-oxamide, has been used.

METHOD.—A Formalin-fixed paraffin section of skin is hydrated and placed in 1% nickel sulfate for 15 minutes. It is washed in copper-free tap water for 10 minutes. The section is flooded with 0 1% dithio-oxamide in 70% ethanol and then with dilute ammonia solution. A faint coloring of the section may be seen with some emphasis on nuclei, red cells, muscle fibers and keratohyaline granules.

If immediately after biopsy the fresh skin is placed in dithio-oxamide for a few minutes and momentarily rendered alkaline the nickel will be immobilized as a colored complex, after which fixa

(6) Brit. J Dermat. 68 237 242, July-Aug 1956.

Needle Biopsy of Liver in Eczema was carried out in 44 cases by Cl. Huriez, F Desmons, M Benoit and P Martin (Lille France) in an effort to ascertain the role of hepatic disease in this type of dermatosis.

In constitutional eczemas, atopic dermatitides histopathologic lesions of the liver were almost always absent and function tests normal. In sensitization eczemas histologic signs and disturbances of hepatic function were not frequent (4 of 13 cases) In eight cases, in alcoholic angiocholitic or cardiac subjects, liver changes apparently prolonged eczema and made treatment more difficult In 6 of 10 patients with multiple drug sensitivities, there was hepatic steatosis with anisokaryosis in 4 and nuclear vacuoles in 2. Study of six patients after gold and one after arsenic therapy showed that eczema and erythroderma following metallic therapy are true toxicodermas.

This histologic study of the liver in 44 eczematous patients showed inadequacy of liver function tests in assessment of liver damage. Only 9% had positive Hanger or MacLagan reactions, but histologically only 50% of the livers were normal 31% showed slight and 19% advanced pathologic changes. Hypergammaglobulinemia was most often observed in sensitization eczemas in which liver changes were slight. Increased gamma globulin implies superimposed infection, not hepatic change.

Hepatic puncture is the only method for determining the state of this organ. Biopsy however may show previous or concomitant lesions of the liver which are not responsible for the dermatosis. Such lesions may result from infections previous intoxications, scleroses or aging Additional study is needed to evaluate finally the role of liver damage in various eczemas.

► [The status of the liver in patients with various dermatoses in the past has been studied principally through liver function tests (see, for example, Ayres, Ayres and Mirovich [Arch. Dermat. & Syph. 62:851 1950] Bauer [Australian J. Dermat. 2:69 1953] and Kresbach [Wien klin Wchnschr 66 762, 1954]) The work of Huriez et al provides an additional approach to [illegible] which deserves much further investigation before valid conclusions can be drawn.—Eds.]

Behavior of Renal Glomerular Filtration in Eczematous Patients. Ugo Maragnan and Carla Lenti[1] studied the glo-

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Presse méd. 64 1935 1936, Nov 21, 956

Minerva dermat. 31 44-51, February 1956

B on the right cheek and tissue A on the left cheek of each person, doing 90 rubs in one minute. For the patch tests, the tissues were *moistened, but for the face experiments, they were left dry*

Three of 50 persons or 6% showed sensitivity In all three, there were positive reactions to the patch tests with tissue B and 1% formaldehyde solution, and to the usage test with tissue B There was no reaction to the tissues without the resins It is concluded that facial tissues impregnated with synthetic resins such as urea formaldehyde are capable of sensitizing Since the amount of formaldehyde is small, it is important to do a patch test not only with the suspected material but also with a 1% formaldehyde solution.

► [What chance does the poor unsuspecting consumer have these days? The words pure, safe, sterilized," etc., certainly do not necessarily indicate absence of possible allergens and labels cannot possibly warn of cross-sensitizations.—Eds.]

Patch Test Studies 2. Details of Method and Practical Experience of Pressure Test are presented by Ake I B Fernstrom[1] (Karolinska Hosp Stockholm)

METHOD—A block of sponge plastic 19×19×4 mm. is covered by a 21×21 mm. square of rubber cloth or cellophane on which a square of blotting paper 9×9 mm. is placed, the three forming a unit. A piece of tape is cut and laid adhesive surface up. Patches are placed at 2 cm. intervals along the middle of the tape the sponge blocks meeting the adhesive surface and the blotting paper face up. The squares of blotting paper are then moistened with the respective allergen solutions and the whole tape applied to a suitable site the back or the inner aspect of the arm.

The sponge block exerts some pressure which helps insure occlusion of the patch and good contact between allergen and skin The pressure test is timesaving which is particularly desirable in mass testing Placing material on the tape is a one stage procedure instead of two stage as in the routine method It is concluded that this new method is simpler and less time consuming than the classic methods heretofore employed

► [*Anyone responsible for the preparation, application and removal of* patch tests is interested in technical and timesaving improvements. These "pressure tests" offer the apparent advantage of insuring a more uniform pressure and perhaps better contact of the test material with the skin. It remains to be seen, however whether additional pressure is always desirable. For example, the investigations of A. A. Fisher at the New York Skin and Cancer Unit have shown that even with the conventional patch test method the skin site tested with certain solid substances in some subjects will respond with vesiculobullous reactions caused by pressure effects rather than allergenic properties.—Eds.]

(1) Acta dermat.-venereol. 35 420-428, 1955.

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Behavior of Renal Glomerular Filtration in Eczematous Patients. Ugo Maragnani and Carla Lenti[1] studied the glo-

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Presse méd. 64 1925 1 28, Nov 21, 1956
Minerva dermat. 3 44 51, February 1956.

merular filtration rate on the basis of creatinine clearance during 24 hours in 40 young patients with eczema and unimpaired kidney and liver function and in 20 controls. The filtration rate was reduced in patients the mean being 88 cc. (97 cc in men and 69 cc in women) The values which ranged from 48 to 150 cc were correlated with severity and phase of the eczema they were highest in patients in whom the dermatitis tended to subside, with reabsorption of fluids from the interstices and elimination and lowest in the patients with exudative and extensive eczema. Patients with a glomerular filtration rate below normal during the acute phase had a normal or almost normal rate when the eczema diminished or disappeared The average rate in the controls was 97 cc (102 cc for men and 91 cc for women) with a range of 76-126 cc The diuresis was reduced in the patients because of increased tubular reabsorption of water but mainly because of the lowered glomerular filtration rate. The average urinary output was 880 cc. in men patients and 652 cc in women patients as compared with 1,200 and 915 cc respectively in the controls The mechanism that produces a reduced glomerular filtration in patients with eczema is still unknown but the changes are related to the altered water balance

► [The figures presented do not appear statistically significant. This does not preclude the possibility that there actually may be a disturbance in glomerular filtration in patients with eczema. For critical evaluation of the data one would have to know What type of eczema did the patients have? How extensive were the involved areas? Were the controls subjects without skin disease or did they have noneczematous eruptions and if so what type? How much fluid was lost through the skin? etc., etc. —Eds.]

Nummular Eczema Review of Literature Survey of 516 Case Records and Follow up of 125 Patients. Abraham I Weidman and H Harvey Sawicky[2] (New York Uni Post Grad Med School and Skin and Cancer Unit) suggest that nummular eczema is not a disease entity but rather a symptom complex caused by multiple etiologic factors many of which are obscure The characteristic lesions are discrete coin shaped erythematous plaques studded with small vesicles or papulovesicles with enlargement by confluence with satellite elements or growth of the individual patches The usual affected areas are the extensors of the extremities and

(2) A.M.A. Arch. Dermat. 73 58-65 January 1956.

sometimes the trunk and face. Pruritus, burning and oozing from small puncta are frequently associated. The round or oval patch, which develops quickly may after healing recur at the same site. Accompanying and possibly etiologic cutaneous condition are dryness or asteatosis, decreased resistance of the skin to alkali allergic eczematous diatheses and infections. Included in the differential diagnosis are contact dermatitis dermatophytosis, Sulzberger-Garbe dermatosis and dermatitis herpetiformis.

Records of 516 cases were reviewed and 125 patients were studied in an eight year follow-up Nummular eczema is most frequently seen in the younger and middle-aged groups about equally divided between the sexes. In decreasing order the dorsa of the hands and fingers extensor surfaces of the forearms legs and thighs, and, infrequently the trunk and face are involved. Patients are usually worse in the winter and better in the summer Of the patients followed, 75% had positive reactions to potassium iodide patch tests (33% potassium iodide in petrolatum) and 72% to potassium bromide Patients with other dermatoses showed a positive patch test reaction to potassium iodide (47%) and to potassium bromide (26%) indicating little specificity for the halogen test Only 11% of patients followed gave a history of allergy and 15 reported allergy in their family insufficient to relate nummular eczema to atopic dermatitis. Most cases were observed in housewives and manual laborers although the selection of cases in the clinic came from these groups rather than from executives or professional people The most satisfactory topical remedies were vioform the tar or hydrocortisone combined with an antibiotic.

► [Positive patch tests with KI and KB are not diagnostic for nummular eczema or for dermatitis herpetiformis, as is shown once more by the fact that half the psoriasis and alopecia areata patients tested by the authors also reacted to patch tests with KI and/or KB Nevertheless it is interesting that the incidence of positive reactions was higher in these diseases than in the other dermatoses in the authors' series The significance of this finding, to our knowledge, is only partially understood Felsher showed that this type of hypersensitivity is not limited to KI and KBr but can be elicited by many substances and is function of the ability of various agents to promote swelling of the collagen of the cutis (J Invest. Dermat. 8 35-55 1947

The sensitivity to KI and KBr does not mean that topical medicaments containing organic compounds with iodine in the molecule, such as iodochlorohydroxyquinoline (vioform) cannot be used in the management of nummular eczema. On the contrary as pointed out by the authors

and corroborated by our own experience, vioform® and related compounds at times are excellent therapeutic agents. Exceptional patients, however with dermatitis herpetiformis are said to have been intolerant to the topical application of vioform® and related compounds.

Agents given systemically which are also of help in managing some cases of nummular eczema are the wide spectrum antibiotics and corticosteroids of the cortisone series.—Eds.]

Local Microbial Origin of Hyaluronidase in Eczema was investigated by A Delmotte[3] (Univ of Brussels) Because the presence of a diffusion factor in eczematous secretions had been demonstrated, and it had been assumed by Charpy that this diffusion factor might be hyaluronidase Delmotte investigated 63 patients with acute eczema, 30 with pyogenic dermatoses and 30 with ulcerations and leg ulcers, as well as the normal skin of the wrist of 9 healthy persons.

Eczematous secretions pus from pyogenic dermatoses and secretions from ulcerations were obtained, using a sterile sponge. The sponge was placed in a Petri dish containing blood agar Bacterial growths were identified and the presence of hyaluronidase in culture was evidenced

Of 33 cases of acute eczema, hyaluronidase-producing bacterial strains were isolated in 92% In 30 cases of pyogenic dermatoses and in 30 of ulcerations and ulcer of the leg they were found only in 60% The skin of the wrist of healthy test persons did not shelter these bacterial strains Whenever pyogenic dermatoses (two cases) or leg ulcers (three cases) underwent eczematization the lesions contained bacteria that produced hyaluronidase The diffusion factor in eczematous secretions may be a bacterial hyaluronidase of local origin

► [An interesting finding Studies are necessary however to ascertain whether or not the hyaluronidase produced by the bacterial flora of the particular lesions plays a role in eczematization. It appears entirely possible that the eczematized terrain merely furnishes suitable soil for the growth of hyaluronidase-producing organisms. Investigations by Prose and the senior editor (J Invest Dermat. 16 169 1951) demonstrated the absence of hyaluronidase activity in allergic eczematous contact dermatitis and in allergic eczematous patch test reactions.—Eds.]

Studies on Clinical Manifestations and Pathogenesis of Microbial Eczema.—*III Exanthematous dispersion (microbids)* are discussed by H Rockl[4] (Univ of Munich) in a further report on the clinical appearance and pathogenesis of microbial eczema. During the course of this type of eczema, sudden dissemination occurs which coincides with the

(3) Dermatologica 111 313-315 November 1955.
(4) Hautarzt 7 70-76, February 1956.

exacerbation of the primary lesion. The dissemination does not affect adjacent but rather distant areas (secondary reactions of Ravaut, id reactions of J Jadassohn)

These eczematoid microbids are of allergic nature and due to the transport of live or dead material via the blood or

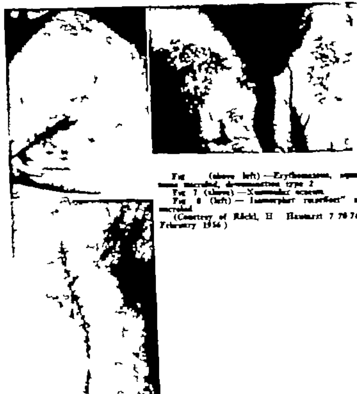


Fig (above left) —Erythematous, squamous microbid, dissemination type 2
Fig 7 (above) —[illegible] eczema
Fig 8 (left) — Isomorphic reaction" in microbid
(Courtesy of Röckl, H Hautarzt 7 70 76, February 1956)

lymph tream into the highly sensiti ed kin They commonly occur during the course f m crobial eczema, but lso ppear after an internal coccogenic focal fection Clin ically two ma n types are observed (1) an erythematous, squamous type characterized by well defined coinl ke, erythematous, squamous lesion resembling those of pityriasis rosea or seborrheic dermatitis, appeari g chiefly on the face, neck and shoulders (Fig 6) (2) more common papulo-

vesicular type characterized by pinhead to grain-sized, bright red papules topped by a small vesicle, appearing in follicular dissemination (cutis anserina like) and forming rather well defined plaques (nummular microbids) (Fig 7) The latter type is often resistant to therapy Not uncommon is an isomorphic effect, appearing in normal skin (Fig 8) and caused by nonspecific stimuli such as scratching and chafing Transitory or combined types are rather rare e.g urticarial papulopustular and erythema exudativum multiforme-like lesions

Histologic study reveals, mainly two types of changes that are not uniform circumscribed lymphocytic spongiosis in the middle and lower epidermis and subcorneal pyknotic spongiotic vesicles (vésiculette primordiale of Civatte) In most cases the vesicles contain leukocytes with segmented nuclei occasionally also eosinophils The epidermis shows moderate acanthosis and the corium rather massive mainly perivascular lymphocytic leukocytic infiltrates The former type is considered allergic and the latter toxic in nature

Three types of dissemination are observed (1) microbids localized around the primary plaque, as in pyoderma, abscesses ulcus cruris etc (2) symmetrical microbids appearing on intertriginous areas (axillae, submammary abdominal folds in obese patient inguinal and genitocrural folds) head and neck regions and flexor surfaces of forearms and wrists (3) symmetrical microbids appearing on trunk or involving the entire skin surface.

In most cases observed the primary plaque was a dermoepidermitis situated on the legs

II Bacterial flora of eczematous skin epicutaneous patch tests with bacteria and broth culture filtrates were studied by Rockl[5] Eczematous skin particularly oozing and crusted patches and dermoepidermitis of the legs contained an abundance of bacteria, which was less pronounced in erythematous scaly psoriasiform and lichenoid eczemas. In acute contact dermatitis and in nummular eczema, involved and surrounding areas contained approximately the same amount of bacteria Bacterial flora of eczematous skin differed qualitatively little from that of normal skin but quantitatively showed Staphylococcus aureus hemolyticus in 94 % patients

(5) Hautarzt 7 113-118, March, 1956

Streptococcus hemolyticus in 27% Str anhemolyticus in 7% and bacteria of the enterococcus group in 26% In 95 tested patients, Bacillus diphtheriae was not found.

In epicutaneous patch testing the method of Storck was used. The only difference was that instead of polyvalent bouillon cultures and bouillon culture filtrates, strains isolated from each case and their bouillon culture filtrates were tested, and nutrient bouillon was used instead of Rosenow bouillon. Epicutaneous patch tests carried out with living bacteria, using the *material lightly innocted together* with glass wool, were mostly positive with Staph. aureus hemolyticus (84%) less often with Str hemolyticus (14%) and rarely with Staph. albus, Escherichia coli, enterococci sarcinae, Pseudomonas pyocyanea and Proteus vulgaris, which had no significance for the pathogenesis of eczema. Of 46 pat ents on whom epicutaneous patch tests were carried out w th l ing and with heat-destroyed bacteria only 6 (13%) showed positive reactions with killed bacteria accord ngly it was concluded that eczematogens are bound to living bac teria wh ch are apt to multiply and to form toxins Posit ve eactions were obtained also with bouillon culture filtrates n 48% of patients 10% reacted equally strong to bacterial strain a d filtrate 47% to the strain only and 26% str nger t the strain than to the filtrate. Cutaneous reactions thus obtained revealed cl nically and histologically the charac teristic features of dermat tis.

Simultaneous ep cutaneous patch testing on controls w th normal kin yielded a high percentage of pos tive reactions. Twent -six patients had strongly positive reaction to living taph lococcic stra ns th two controls with healthy kin showed more or less strongly positive ep cutaneous reac tions 21 times Fourteen patients had positive eaction to bouillon culture filtrates the two controls tested had eight posit reaction Because of positi reaction in the con trols, a pecifi sensitizatio can hardly be assumed. Rather th h pothes i accepted that nearly everyone may be a potent al micr bial eczematic

* [Another attempt to investigate the role of bacteria as allergens in eczematous eruptions. The data presented here are similar to the many previous tudies on the same subject, e., they do not prove that bacteria are important as causal or contributory allergenic agents. They show that, uld be expected, the damaged skin areas provide favorable culture

medium for large quantities of bacteria but there is no qualitative difference in the bacterial flora of eczematous and normal skin, nor is there any greater skin sensitivity to these bacteria in persons with eczematous eruptions than in control subjects.

All of this of course does not rule out the possibility that bacteria actually may play a more or less important role in the causation or maintenance of certain eczematous eruptions, but convincing proof for such action is still lacking —Eds.]

Allergic Dermatoses Due to Foods Roentgen Findings of Clinically Silent Gastrointestinal Reactions are reported by Giuseppe Zina Giovanni Bonu and Giuseppe Lovera[6] (Univ of Turin) The allergic pathogenesis of gastrointestinal symptoms and their causative agent is difficult to determine, but systematic roentgenography reveals variations in evacuation of the stomach and small intestine and frequent jejunoileocolic dyskinesias after ingestion of the suspected allergen. The motility of the digestive tract may be studied at fixed times on a roentgenogram taken after ingestion of contrast medium and on another roentgenogram a few days later at corresponding times after ingestion of contrast medium with the suspected allergen The specificity of changes observed should be confirmed by a third roentgenogram after ingestion of contrast medium with well tolerated foods

This method was used in five persons in whom the suspected allergen had never produced manifest subjective or objective gastrointestinal symptoms although it had caused intense skin reactions in the form of chronic urticaria or chronic eczema. The eczema was resistant to treatment mainly because it was not known to be caused by foods used in the daily diet All roentgenograms showed pronounced gastrointestinal changes after ingestion of the allergen The same changes were also observed after subcutaneous injection of the standard extract or a mixture of standard extracts, of food or of foods which skin tests and previous roentgen studies had indicated as the causative factor

Studies of Besnier's Prurigo (Atopic Dermatitis) on 311 patients are presented by Sven Hellerstrom and Hjordis Ladman[7] (Karolinska Hosp Stockholm) This condition accounts for one fifth to one sixth of all patients treated for skin disease at this clinic Incidence appears to be increasing possibly due to increase of allergenic and skin sensitizing factors

(6) Minerva dermat 31 228-234 August 1956
(7) Acta dermat. venereol. 36 11 22 1956

Age at onset was under 1 year in 40% of patients and from 1 to 5 years in another 40%. Only 69 patients did not mention familial occurrence of asthma, hay fever, allergic rhinitis and prurigo Besnier. Most patients improved in summer and were usually worse in autumn and spring. In one series all patients reported exacerbations during menstruation, but 11 of 14 improved during pregnancy. Where summer exacerbations occurred they were believed due to pollen hypersensitivity. The number of circulating eosinophils in the blood is often high in prurigo Besnier, although it is not diagnostically specific. Eosinophilia on hospitalization was significantly higher than on discharge after clinical improvement. Correlation between skin tests and heredity showed 206 patients with positive skin tests and positive heredity, 16 with negative skin tests and positive heredity, 56 with negative heredity and positive skin tests and 6 with negative heredity and skin tests. Because of its chronic and disabling character and its incidence in all strata of society, prurigo Besnier is an important disease.

► [The figures on the familial occurrence of allergic asthma, allergic rhinitis and atopic dermatitis in patients with atopic dermatitis are very close to those published by the senior editor in *Atopic Dermatitis* (New York: New York University Press, 1955). In his series of 150 consecutive cases of atopic dermatitis, 62% gave a family history of atopic diseases. In 31% there was a personal history of allergic asthma and allergic rhinitis and only 21% had neither a familial nor personal history of these diseases.—*Eds.*]

Constitutional Problem in Neurodermatitis. Since neurodermatitis (flat, exudative eczematoid Rost, endogenous eczema, atopic dermatitis and others) was differentiated from eczema and considered an entity, many constitutional details have been reported by clinical observers, e.g., oblong, pinched face and long, thin hands, asthenic or leptosomic habitus and leptosomic features with an athletic component. As anthropologic serial measurements had not been carried out in neurodermatitis patients, Siegfried Borelli and Johann S. Kraft (Univ. of Munich) studied 41 from Hamburg (north Germany) and 49 from Munich (south Germany). Body height, distance of upper sternal edge and upper symphysial edge from the floor, circumference, breadth and depth of chest, shoulder and pelvic width and length of anterior wall of trunk were measured. From these figures, 11 body indexes can be computed and compared with the scheme of Plattner

(W) [illegible] 113 44, April, 1956

In each patient six or three indexes were calculated, of which two or one was "habitus typical" for one of the various somatic types and "habitus tropic" for two others. Thus it was possible to include the patient in one type and also to determine the relations to the two other habitus types. About 61% of the patients had a leptosomatic or mainly leptosomatic habitus, 15.5% an athletic (normally both together only 40-50%), 8.2% a pyknic (normally far above 20%) and 2.1% an atypical (normally about 6.6%) habitus. These results were markedly different from average figures found in the European population. They cannot be considered alone but must be correlated with the various other somatic and psychic peculiarities observed in neurodermatitis patients.

New Serologic Method to Ascertain Sensitization to Allergens. Two in vitro methods for determination of antigens have been described, e.g., the thrombocyte agglutination test and a serologic nephelometric method based on the specific turbidity reaction between the serum of sensitized persons and allergen. Two serum factors are responsible for the turbidity reaction: specific factor I, which is thermolabile and dialyzable through semipermeable membranes, e.g., cellophane, and unspecific nondialyzable factor II, which is found regularly in the serum of sensitized and nonsensitized persons and in some animal serums.

R. Hoigné[9] (Univ. of Zurich) describes a third factor which inhibits the turbidity reaction. Turbidity was observed in freshly drawn serum after addition of allergen but not in serum which was used six to eight hours after it was drawn. By the aid of dialysis and heat, specific factor III (B+N) could be separated. It is thermostable and dialyzable and consists of two components, of which B specifically blocks factor II and N neutralizes allergen. Factor III (B+N) exists in three phases: an inactive phase (profactor III), an active free form and a combined form with factor II. Component N is present in fresh serum; component B can be demonstrated only after storage for at least six to eight hours at room temperature. Its precursor is called component A. Both factors I and III (B+N) are specific and dialyzable through cellophane membrane, thus permitting the conclusion that factors I and III are not proteins, in contrast to

(9) Schweiz. med. Wchnschr. 85: 1272-1274, Dec. 27, 1955.

classic antibod es which are proteins chiefly gamma globulins, and not dialyzable.

The various factors in the serum of sensitized persons may be isolated by (1) measuring the turbidity reaction between allergen and serum factors with a sensitive nephelometer (2) exposing the filtrate dialyzate or serum to heat of 56 C. f r 20 minutes, and (3) incubating the mixtures of factors at room temperature. Specific turbidity reaction tests were done on 111 patients with drug inhalant or food allergies. The res lts corresponded well to clinically implicated aller gens in these pat ents.

► [The editors have not had the opportunity to test this and the other new in itro methods for demonstration of antibodies developed by Holgrof, Storck and associates. Apparently the technical difficulties inherent in these methods thus far ha interfered with widespread trials elsewhere. —Eds.]

Generalized "Ids (Autosensitization") in Varicose Eczema. H Haxthausen (Copenhagen) found secondary eruption so common in aricose eczema as to constitute an mportant ymptom. Of 99 males and 136 females with vari cose a d post thrombotic eczemas 37% had secondary eruptions, compared with 4% of 522 male and 519 female controls with other forms of eczema.

The primary eczema may be dry or oozing widespread or limited. U ually the lesions ha been scrat hed and lichenification results, or they ha e been ubjected to irritating local medication. Th generali ed eruption is strikingly sym metrical—a conseq ence of its hematogenous origin. Itching ften moderate The primary lesion is a ves copapule with a preponderance f vesiculation although there are many ariation from erythematous scaly patches milar to p ty riasi rosea t areas f l henification resembl ng prurigo nodules. There i a predilection for the flexor surface of the forea m (Fig 9) and, with decreasing frequency the thighs leg tru k f ce, hands, neck nd feet The kin surrounding the primary eczema is seldom affected. Microscopically th picture corresponded to that of primary acut ec zema w th pongios f the ep dermal ll and eczematous es ulat on mild ed ma f the upper corium and perivascular infiltrations, predominantly lymphocytic

An planation of the pathogenesi of these d eruption

Acta dermat venereol 35 271 280, 1955

is complicated by local infection with bacteria or fungi and local treatment with substances which may induce allergy Varicose and thrombophlebitic eczemas are distinguished by circulatory disturbance. With high hydrostatic pressure in the blood vessels filtration edema occurs and the dermal cells and tissues are damaged probably from enzymatic autolysis

When the primary eczema is adequately treated—preferably by bed rest to permit circulatory compensation—the secondary eruption usually subsides spontaneously Zinc lin-

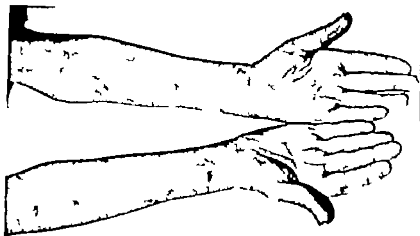


Fig 9 —Generalized eruption of common vesicopapular varicose eczema, showing favorite localization to forearms. (Courtesy of Harthausen, H. Acta dermat venereol. 35:271-280 1955)

iment is used topically tar being reserved for advanced cases of the scaly pruriginous variety Of some 88 patients 19 were readmitted with recurrent eczema of the legs 11 had a generalized eruption and 8 had no generalization It is concluded that recurrence is common and that immunity does not follow the generalized eruption

► [An excellent description of a rather common and characteristic syndrome. While the words "id" and autosensitization dermatitis are used by most dermatologists in naming the eruptions on the arms and other areas secondary to varicose eczemas, adequate scientific evidence in support of these concepts is not yet available —Eds.]

Pathogenesis of Eosinophilic Pneumonitis (Löffler's Syndrome) was studied by William L Epstein and Albert M Kligman[2] (Univ of Pennsylvania) who observed eosino-

(2) J.A.M.A. 162:95-97 Sept. 8, 1956

philia, up to 80% in seven patients hospitalized for pneumonitis with findings characteristic of Loffler's syndrome viz., a patchy migratory infiltration seen in serial chest x rays. Each patient had received from two to six graded injections of 3-pentadecylcatechol in sesame oil for prophylaxis against poison ivy dermatitis. Cough, dyspnea, malaise and fever began 8-48 hours after the last injection. Sharp chest pains, production of sputum, occasional rales and sometimes an inflamed pharynx were found. The only consistent features were eosinophilia and pneumonitis. The latter cleared in 4-15 days.

The eosinophilia in the lungs may be due to the fact that these organs and, less importantly other viscera tend to trap or filter eosinophils in some unknown way possibly because eosinophils have an affinity for structures with high histamine reserves, of which the lung is supposed to be one. The varying degrees of eosinophilia in allergic and parasitic diseases would explain mild abortive forms of pneumonitis and pulmonary infiltrations massive and dense enough to be revealed by x rays.

► (The occurrence of Loffler's syndrome in these cases does not come as great surprise. Loffler's syndrome as part of an allergic drug reaction has been repeatedly described. What comes as a surprise is that the authors did not observe vesicular eruptions of the hands and feet, erythema multiforme-like eruptions, or other eruptions which are seen sometimes when excessively large doses of "natural" poison ivy extracts are given. —Eds.)

Erythema Neonatorum was studied by Jerome R. Harris and Bela Schick[3] (Beth-El Hosp., Brooklyn) in 75 newborns. The rash began on the face especially the cheeks, and spread rapidly to the forehead and centrifugally to the extremities. Its color ranged from pink to scarlet. In a few hours macules of varied size appeared on the cheeks and spread downward to the body (Fig 10). Occasionally the erythema persisted two to three days before macules developed. Not uncommonly the smallest macules appeared without previous erythema and tended to be more scattered, fewer in number and sharply demarcated. Typical macules were large and dark with irregular margins which blended into the surrounding erythema or stood in sharp contrast to the unaffected skin. Pustules occurred only after papules had developed. Actually a more circumscribed and elevated form of the papule, they were found most frequently on the back, buttocks and ab-

[3] A.M.A. J. Dis. Child. 9: 27-33, July 1956.

is complicated by local infection with bacteria or fungi and local treatment with substances which may induce allergy. Varicose and thrombophlebitic eczemas are distinguished by circulatory disturbance. With high hydrostatic pressure in the blood vessels filtration edema occurs and the dermal cells and tissues are damaged probably from enzymatic autolysis.

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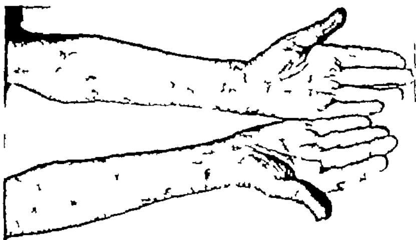


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presumably nonallergic dermatoses associated with blood or local eosinophilia.—Eds.]

3 DRUG ERUPTIONS

Skin Necrosis Following Intravenous Use of Nor Epinephrine. Nor-epinephrine, administered intravenously is being used widely in treatment of shock and peripheral circulatory collapse. In an extremity receiving nor epinephrine infusion there is frequently blanching of the skin at the point of injection and occasionally along the vein being used. Sometimes the area about the vein becomes red and hard as in phlebitis. Usually this subsides shortly after infusion is discontinued, but may remain for 24-48 hours. In a few instances the blanched area becomes cyanotic and anesthetic. The bluish purple color does not disappear on pressure, and in 48-72 hours vesicles containing clear yellow fluid develop. This is followed by gangrene of the skin and subcutaneous tissue, with irregular but sharply demarcated borders. The surrounding skin may be hyperemic. Richard A. Shapiro and Samuel Perlow[1] (Michael Reese Hosp.) report six cases of gangrene of the skin after nor epinephrine therapy.

Animal experiments indicate that perfusion of nor epinephrine solution through an undamaged vein wall is possible with sluggish circulation and stagnation of blood in the veins, as is usually present in shocklike states. The acute venous spasm which so commonly occurs after the first rapid influx of the nor-epinephrine solution may intensify such stagnation. Injection of a small amount of a nonpressor solution overcomes the obstruction and reinstitutes the flow. If venous spasm follows, the flow should be slowed. Application of warm compresses along the course of the vein and injection of a small amount of procaine into the tubing may be helpful. Insertion of a cannula, or a fine polyethylene catheter high into the vein of the extremity where flow is more rapid than in the peripheral vessels and where the solution is quickly diluted by the large blood volume, and elevation of the extremity to aid venous return should prevent necrosis due to venous stasis of the solution. When no

[1] Am. J. Surg. 92:566-570, October 1956.

domen were 2-4 mm in diameter and were gray or yellow Untouched they were resorbed completely within 24-48 hours. Both papules and pustules disappeared first from the areas least involved remaining longer where they were in greater concentration especially the back and buttocks.

When total eosinophilic and white blood cell counts were done largely over the first four days of life and representing each stage of the rash the eosinophil count was found to be related to the rash Infants with pustules had significant eosinophilia compared with babies with no rash. This difference diminished when the allergic skin response was milder

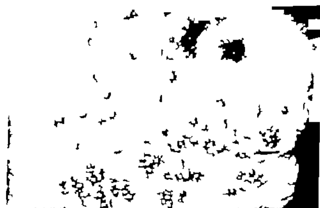


FIG. 10 Crop of papules centrally placed in areas of erythema. (Courtesy of Harris, J R and Schick, B. A.M.A. J Dis. Child. 92 27 33 July 1956)

(papules or macules) It is suggested that erythema neonatorum might be the reason for the wide eosinophil range reported for newborn infants

The rash is probably due to specific sensitization of the baby to a maternal protein substance passed across the placenta

► [This type of eruption in the newborn has been described in the literature under a variety of names. The finding of Harris and Schick that there is a local and blood eosinophilia and that the intensity of the eosinophilia is closely correlated with the severity of the eruption is new and highly interesting

One may question, however the justification for interpreting this type of eruption as an allergic one and even more so the speculation that the allergy is to maternal proteins. Dermatologists are well acquainted with the fact that neither local eosinophilia nor blood eosinophilia necessarily indicates that a cutaneous lesion is based on allergic sensitization. Dermatitis herpetiformis and eosinophilic granuloma are pertinent examples f

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( ) Am. J. Surg. 92:366-370, October 1956.

epinephrine is required only intermittently and the catheter is kept in the vein for immediate availability it would be advisable to flush out the vein with saline via a three-way stopcock in the intravenous system to prevent stagnation of nor epinephrine in the vein

► [The clinical picture of bulla formation followed by necrosis of rather sharply delimited areas is not unlike that of embolia cutis medicamentosa following the direct intra arterial injection of certain materials. In the cases of Shapiro and Perlow however leakage from the venous structures apparently must first take place into the surrounding tissues.—Eds.]

Skin Sloughs Associated in Levophed [a] Pathogenesis, Prevention and Treatment. Levarterenol (levophed[r]) acts *as a powerful vasopressor by causing generalized vasocon*striction Its most common detrimental side effect is necrosis of overlying skin when the solution is accidentally extravasated. Skin necrosis has also been reported at sites distant from the point of infusion along the course of the vein when no extravasation has occurred This has been seen only in lower limbs with already impaired arterial supply

In experimental studies Joseph T McGinn and Joseph Schluger[5] (Long Island College Hosp Brooklyn) found that continued infusion of levarterenol is necessary to produce gangrene. The period during which the drug is presented to the tissue appears more important than total dosage or concentration Meticulous observation of the infusion site and course of the vein would probably detect the early pallor frigor and induration in time to avert irreversible changes If any of these signs of local vasospasm and ischemia due to levarterenol are observed, the infusion site should be changed As soon as possible phentolamine should be injected subcutaneously throughout the affected area For adequate penetration 5 mg phentolamine may be dissolved in 15-20 cc normal saline and 125 turbidity reducing units of hyaluronidase added. In one patient it was possible to continue levarterenol infusion after the blanched area was treated with phentolamine without changing the infusion site

Phentolamine produces initial vasodilatation lasting up to 10 minutes followed by adrenergic block for several hours During this period, blood vessels of the skin should be insensitive to extravasated levarterenol Thus, the possibility exists of continuing infusions through catheters after pro-

(5) Am. J Surg 92:594-602 October 1956

tection with phentolamine when it is definitely known there is no gross extravasation.

I all patients receiving levarterenol treated with locally injected phentolamine, blood pressure was unaffected. From the authors experience in man and animals, it appears that phentolamine, administered shortly after levarterenol extravasation, completely prevents irreversible damage.

Hyperergic Panvasculitis with Clinical Appearance of Multiple Gangrene of Skin is described by Heinz Langhof[41] (U v of Greifswald)

Woman, 73 In 1952 had multiple cutaneous gangrene following an attack of grippe and preceded by urticarial erythema. Uropor



Fig —Relapse of cutaneous necroses in 1955. (Courtesy of Langhof, H Arch. klin exper Dermat 202 331-338, 1956.

phyrin 1+ and coproporphyrin 3+ wer found in the urine. During summer 1952 and spring 1953 she was hypersensitive to sunlight. I summer 1954 and April 1955 she had epeated grippal infec tions. During April barbiturate compound was taken (0.25 Gm. kalypnon 10 times in 12 days) 10 days after the first dose an urticarial intensely itching erythema appeared on exposed parts and hanged into hemorrhagic necroses within 3 day The urine wa dark brownish red. On hospitalization, temperature was 100 F pulse rate 120 and blood pressure 130/95 She tended to collapse and had intense pains in the upper abdomen (ntestinal spasms in porphyrinuria?) Lentil-to penny-sized hemorrhagic cutaneous nec roses were seen. Some er firm, depressed, cool and extremely sensitive others showed flaccid, hemorrhagic blisters (Fig 11)

Blood study showed sedimentation rate 80/104 3,580,000 ed

41 Arch klin exper Dermat 202 331 338, 1956

blood cells 65% hemoglobin color index 0.9 11% reticulocytes, anisocytosis and poikilocytosis 252,700 thrombocytes bleeding time 80 seconds coagulation time 213 seconds 3,000 white blood cells, with 2% juvenile, 3% stab and 3% segmented cells, 72% lymphocytes and 20% monocytes. There was intensive toxic granulation of neutrophils. Three days later the white blood cell count was only 2,400 with 1% stab and 2% segmented cells, 66% lymphocytes and 31% monocytes. The blood group was AB Rh+ Total serum proteins were 6.91 Gm./100 ml (43.9% albumin and 5% alpha$_1$ 11.4% alpha$_2$, 13.5% beta and 26.2% gamma globulin) The result of the Takata Ara test was 50 mg./100 ml. and of the Weltmann test, 5% Nonprotein nitrogen measured 40 mg./100 ml., calcium, 8.7 mg., potassium 22 mg sodium chloride 590 mg and bilirubin 0.6 mg Urinalysis revealed a few leukocytes in the sediment, traces of urobilin, 3+ urobilinogen, 1+ uroporphyrin and 3+ coproporphyrin. The urine was dark brown red 17 ketosteroid excretion was 12.6 mg one month later it was 6.8 mg

With the disappearance of abnormal porphyrinuria, the granulocytes increased (3 400 white blood cells, with 3% juvenile 19% stab and 34% segmented cells, 40% lymphocytes and 4% monocytes) After agranulocytosis disappeared with iron therapy tests with salicylic acid and kalypnon were carried out 0.250 Gm. of the latter caused copro- and uroporphyrinuria on the same day Three hours after intake, the white blood cell count had decreased from 5,200 to 2,000 and the granulocytes from 52% to 16% but the skin remained normal. Seven hours after exposure to sunlight an intensive erythema appeared on exposed parts of the back i.e., light sensitivity was increased again.

Histologically nonhemorrhagic urticarial lesions revealed endothelial swelling of the capillaries and dense perivascular infiltrates, consisting of granulocytes, the nuclei of which were breaking down (leukocytolysis) Peripheral parts of hemorrhagic necroses showed dense infiltration by erythrocytes, destruction of all layers of vascular walls, disintegration of tissue fibrils and necrosis extending into the subcutis. All these findings corresponded to the Arthus phenomenon.

Because of coexisting agranulocytosis results of Vaughan's test (which proved barbiturate hypersensitivity with diminution of granulocytes) increased gamma globulins and serum potassium low serum calcium and these same findings histologically the condition was assumed to be one of hyperergic cutaneous subcutaneous panvasculitis. Localization of necroses can be ascribed to light hypersensitivity since only exposed parts were involved and light sensitivity had repeatedly caused light dermatitis The appearance of necroses may be explained by light and additional vasoconstrictor action (porphyrin low serum calcium) Perivascular accu

mulation of granulocytes corresponds to present view on agranulocytosis in which antigen-antibody reaction causes agglutination of granulocytes at the periphery. Granulocytes then incur autolysis and set proteinases free, which may account for pruritic and urticarial phenomena.

Study of the Sensitizing Potential of Novobiocin was made by Henry Welch, C. N. Lewis, L. E. Putnam and W. A. Randall[7] (Food and Drug Admin.) in 208 men given 10 Gm. orally over 12 days. Only one had a drug rash (less than 0.5%). Yellow discoloration of the scleras occurred in three patients, but faded gradually on discontinuation of the drug. There is evidence that this discoloration results from yellow pigment produced by the metabolism of novobiocin. These subjects showed no other symptoms to suggest true jaundice. The relatively high percentage of skin rashes reported during early clinical use of novobiocin may be related to the dose and number of days of treatment.

Novobiocin produces high blood concentrations after oral administration. These concentrations are probably considerably higher than those obtained by oral administration of any other antibiotic with similar doses. Blood concentrations vary from person to person and even in the same person after similar doses. However, in none of the subjects did the variation result in blood concentrations too low to be effective against bacteria susceptible to novobiocin.

Novobiocin is probably bound up to 90% by plasma proteins and only small amounts are excreted in active form. It seems quite possible that through close and relatively prolonged contact with the body proteins partial antigens are formed, which in turn evoke the sensitizing phenomena that has resulted in the relatively high percentage of skin rashes reported in the early clinical use of this drug.

Because of the relatively high activity of novobiocin against susceptible micro-organisms and the extremely high blood concentrations obtained with relatively low doses of this drug, it is proposed that doses of 0.5 Gm. twice daily should be ample for most susceptible infections. Through use of such a regimen, annoying skin rashes previously reported with this drug may be kept at a minimum.

* (The editors have abandoned the use of novobiocin because of an inci-

7) Antibiotic Med. & Clin. Therapy 3:37-42, June, 1956.

dence of skin eruptions experienced by about 30% of patients on doses of 750 to 1 000 mg daily and because even in such relatively large doses this antibiotic failed to control acne in several patients who subsequently were adequately controlled by the same dose of tetracycline.—Eds.]

Erythema Multiforme Following Ingestion of Tetracycline was observed by Carlos A Castanedo and José Mesa Ramos[8] in two patients who had taken tetracycline, chlortetracycline or both One appeared to tolerate oxytetracycline but had two episodes of erythema after ingestion of capsules or tablets of tetracycline from different commercial sources. The possibility that the skin reaction was produced by coloring matter in the capsules or tablets was considered. Information from one manufacturer stated that the color used was tartrazine or "hydrazine yellow (Merck) Similar data regarding the other preparation used were unavailable. The authors believe that the reaction was most likely due to the drug itself

► [In our own experience the incidence of allergic dermatitis following the systemic use of the tetracycline antibiotics has been practically nil. —Eds.]

Acneform Eruption Due to Corticotropin is distinguished from acne vulgaris by Maurice Sullivan and Israel Zeligman[9] (Johns Hopkins Hosp) Clinically corticotropin eruption can occur at any age evolves rapidly is of short duration and involutes rapidly after withdrawal of the drug This is in contrast to acne vulgaris which occurs in teen-agers or young adults evolves slowly is of long duration and usually involutes slowly In ACTH eruption, the skin is dry and the lesions small seldom larger than 2 mm whereas in acne vulgaris the skin is oily and the lesions may be 5 mm to 3 cm if cystic The primary lesions of ACTH eruption are diffusely distributed uniform follicular papules and pustules (Fig 12) Microscopically the two diseases show hyperkeratinization of the follicular orifice followed by formation of an epithelial cyst perifollicular cellular infiltration and, in some cases by foreign body type granulation tissue and suppuration They differ microscopically in that the lesion of acne vulgaris is larger abscess formation is more common and extensive and the sebaceous glands are hyperplastic in contrast to the normal appearance of the sebaceous glands in ACTH eruption

(8) Bol. Soc. cubana dermat y sif 12 247 248, December 1955
(9) A.M.A. Arch. Dermat. 73 133-141 February 1956.

These d fferential findings signify two disturbances contributing to the initiation of acne vulgaris—abnormal keratinization of the occluded follicle and hyperplasia of the sebaceous glands. Rothman bel eves that lack of sebaceous hyperplasia in the ACTH condition indicates that these glands are not stimulated by the adrenal cortex. It is suggested on the basis of animal experiments that testosterone



F —Acneform eruption due to ACTH, showing diffuse distribution of small, uniform follicular papules and pustules. (Courtesy of Sullivan, M., and Zeligman, I A M Arch Dermat 73 1[illegible] 1, February 19[illegible].)

causes eba eou gland hyperpla ia in the male nd progesterone causes t in the female. It is postulated that acne vul garis depend on a elati e or absolut crease in the ratio f androgens and/ progesterone to estrogens. The follicular keratinizing factor in both eruption stimulated by ACTH In ddition f t saprophyte, the partially anaerob acne bacillus, reported orginally by Unna n every comedo f cn ulgaris, may be respons ble for the greater tendency d acne lgaris to form abscesses. If the acne bacillus is a f ct pust lation, the fatty culture medium probably ;

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nut Creek, Calif) report the occurrence of nonthrombocytopenic strongly pruritic erythematopurpuric eruptions in three patients following intake of miltown a drug chemically identical with equanil,* two tranquilizers which have been indiscriminately and widely used. Capillary fragility tests were positive other clinical findings, including blood counts, were negative. One patient had an eruption a few hours after ingestion of the first tablet (400 mg) of miltown.

Reactions to Chloral Hydrate. Herbert B Christianson and Harold O Perry[3] (Mayo Clinic and Found.) report data on seven patients, aged 29-70 with allergic cutaneous reactions and two aged 26 and 81 with somnambulistic reactions to chloral hydrate. Seven had an allergic background.

The commonest skin manifestations of hypersensitivity to chloral hydrate are erythema, exanthemas (scarlatiniform) urticaria and eczematoid dermatitis. The eruption usually begins on the face or back, later involves the neck, chest and arms, finally may become generalized or universal and is followed by desquamation or exfoliation. Fever is fairly common and the patient may be acutely ill. The eruption appears in from several hours to 10 days after ingestion of the drug When the drug is discontinued, the patient ordinarily recovers in 5-10 days. In addition to cutaneous reactions somnambulism may occur

When chloral hydrate is taken in toxic doses, gastrointestinal irritation occurs and the patient may become comatose with relaxation of the musculature hypotension, convulsion delirium and cyanosis Death usually results from cardiorespiratory failure Reactions to chloral hydrate are similar to those of chloroform Chloral hydrate and other chloral derivatives are contraindicated in patients with marked hepatic or renal disease, since they are detoxicated in the liver and kidneys much as chloroform.

The authors suggest the following classification for cutaneous reactions to chloral hydrate (I) erythematous and exanthematous, (II) urticaria and angioneurotic edema (III) hemorrhagic (IV) eczematous, (V) exfoliative dermatitis (VI) erythema multiforme (bullous) (VII) fixed eruptions (VIII) ulcerative (IX) pyoderma like and (X) miscellaneous.

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[3] A.M.A. Arch Dermat. 7 [illegible] September 1956

not adequate in ACTH acneform eruption because of the absence of sebaceous gland hyperplasia

► [The original article has an interesting presentation in tabular form of the clinical and histopathologic differences between acne vulgaris and acneform eruptions due to ACTH It has been our impression that the incidence of acneform eruptions from ACTH perhaps is less now than several years ago While this may be due to the more judicious use of ACTH with smaller doses, improved dosage schedules and newer forms of the product, it is also possible that the newer batches of ACTH are more purified thus containing less of a possible "acnegenic factor That such a factor may be present in "unrefined" and perhaps refined" ACTH, at least must be considered since the investigations of Lasher Lorincz and Rothman (J Invest. Dermat. 24 499 1955) demonstrated the presence of a sebaceous gland tropic (acnegenic) factor in the pituitary gland of mice. —Eds.]

Adverse Reactions to Meprobamate a new tranquilizer are reported by Henry T Friedman and Willard L. Marmelzat[1] (Los Angeles) Five patients had cutaneous eruptions These included widely disseminated or generalized purpuric maculopapular and vesicular eruptions an erythematosquamous rash without purpura and a morbilliform exanthema with a tendency toward confluence. Intense pruritus usually accompanied the skin eruptions. The lesions had a predilection to appear first in the pelvic girdle area genitalia and groins in both males and females The eruption disappeared after cessation of medication or administration of antihistamine and/or corticotropin Repeated intake of meprobamate was followed by relapses An allergic mechanism was considered to be the cause In one patient appearance of the rash six hours after intake of the first tablet suggested a possible cross sensitization to a chemically related compound such as mephenesin Other physicians have had similar experiences with drug eruptions some severe, after meprobamate therapy

In another patient meprobamate therapy was followed by intestinal hyperactivity (severe diarrhea) and in a seventh by diplopia In addition three patients showed paradoxical excitement after use of the drug

► [We have also seen a few cases in which the chronologic sequence of events strongly suggested meprobamate as the cause of the eruption. One of them was an urticaria lasting for several months —Eds.]

Nonthrombocytopenic Purpura Due to Miltown® (2 Methyl-2 N Propyl 1,3 Propanediol Dicarbamate) W J Carmel Jr and T Dannenberg[2] (Kaiser Found Hosp Wal

(1) J.A.M.A. 162 628-630 Oct 13, 1956
(2) New England J Med 255 770-771 Oct. 18, 1956.

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Reactions to Chloral Hydrate. Herbert B Christianson and Harold O Perry[3] (Mayo Clinic and Found.) report data on seven patients, aged 29-70 with allergic cutaneous reac tions and two aged 26 and 81 with somnambulistic reactions to chloral hydrate. Seven had an allergic background.

The commonest skin manifestations of hypersens tivity to chloral hydrate are erythema, exanthemas (scarlatiniform) urticaria and eczematoid dermatitis The eruption usually begins on the face or back, later involves the neck, chest and arms, finally may become generalized or universal and is fol lowed by desquamation o exfoliation. Fever is fairly com mon and the patient may be acutely ill. The eruption appears in from several hours to 10 days after ingestion of the drug When the drug is disco tinued the patient ordinarily recovers in 5-10 days. In addition to cutaneous reactions, somnambuli m may occur

When chloral hydrate is taken in toxic doses, gastrointestinal irritation occurs nd the patient may become comatose with elaxation of the musculature hypotens on convulsions delirium and cyanosis. Death usually results from cardiorespiratory fail re Reactions to chloral hydrate are similar to those of chloroform. Chloral hydrat and other chloral derivatives are contraindicated in patients with marked hepatic or renal d sease since they are detoxicated in the l ver and kidney much a chloroform

The utho suggest th following class fication for cutaneous reactio to chloral hydrate (I) erythematous and exanthemat u (II) urticaria and angioneurotic edema, (III) hemorrhagic (IV) eczematous (V) exfoliative der matitis, (VI) erythema m ltiforme (bullous) (VII) fixed eruptions, (VIII) ulcerat e (IX) pyoderma l ke and (X) miscellaneous

(3) A.M.A. Arch. Dermat. 7 23 348, September 1956

Despite the reactions the authors believe that chloral hydrate is relatively safe and effective

► [We agree with the authors that chloral hydrate has a definite place in the dermatologic armamentarium. It is an effective hypnotic and, as once more evidenced by this article, is one with a very low incidence of adverse reactions.

Chloral hydrate to a limited extent, is used also as a topical medicament, for example, in scalp lotions When topically applied it causes allergic eczematous eruptions in rare instances. Sulzberger and the senior editor reported a case (J Allergy 9:519 1938) in which a patient first developed allergic eczematous contact dermatitis from topically applied chloral hydrate and at a later date an eczematous eruption on the scalp, face hands and forearms following systemic administration of the same drug—Eds]

Clinical and Experimental Investigations on Photodynamic Effects of Phenothiazine Derivatives Particularly of Chlorpromazine were carried out by K H Schulz A Wiskemann and K. Wulf[4] (Univ of Hamburg Eppendorf) Phenothiazine derivatives have been widely used because of their depressing effect on the central nervous system reduction of metabolism and sympathico-parasympathicolytic and histamine-antagonizing effects The most commonly used preparations are multergan phenergan and chlorpromazine All these drugs of which chlorpromazine is Cl substituted in the 3 position often cause side effects many of them cutaneous manifestations primarily allergic in nature. Two groups of skin eruptions can be differentiated. (1) Urticarial, scarlatiniform or morbilliform mostly generalized exanthemas occur in about 10% of patients (mostly women) Sensitization is endogenous (2) Allergic contact dermatitis appears, in which sensitization occurs by exogenous contact and takes place primarily in the epidermis patch tests are mostly positive Incidence is high in nursing personnel from handling tablets ampuls etc. and in patients treated topically with creams containing these drugs.

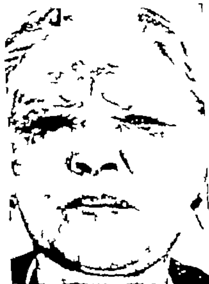
Apart from allergic sensitization phenothiazine derivatives also have photosensitizing effects which in five cases were observed and confirmed by combined patch tests and exposure to light

Woman, 65 employed as a charwoman in the department of internal medicine, had intensive dermatitis with edema of eyelids (Fig 13) Patch tests without irradiation were positive to chlorpromazine patch tests with irradiation showed more intensive reaction to chlorpromazine and other phenothiazine derivatives than

(4) Arch. klin. u. exper Dermat. 202 285 298 1956.

to light alone, although chlorpromazine light sensitivity was marked. Apart from an eczematous allergy in this case photoallergic reaction to chlorpromazine existed, which was engendered and elicited by the drug (previously response to light was normal) and which persisted for months after the last exposure. Similarly in Case 2 photoallergy was assumed.

I the remaining three cases and in fi e control persons phototoxic reactions were seen after irradiation of patch tests with chl rpromazine, which is the most act ve of phe



F 13. Photoallergic eczema following cutaneous contact with chlorpromazine. (Courtesy of Schulz, K. H. et al. Arch. klin. u. exper. Dermat. 203:[illegible], 1956.)

nothiazine deri atives. Prophylacti precautions are suggested for the personnel handling these drugs.

► [An excellent study setting apart several categories of sensitivity engendered by this therapeutically highly valuable group of phenothiazine derivatives: (1) phototoxic reaction, based on the photodynamic action which occurs in all the subjects who were tested. (2) photoallergic reaction in which the patch test with the drug alone is negative but which can be demonstrated by irradiation of the patch test site. (3) photoallergic reaction in combination with an allergic eczematous contact-type sensitization, in which the patch test is positive with the phenothiazine derivative alone but stronger response is elicited if the patch test site is irradiated.

I should be noted that, as was show by Sidi, the often protracted

course of these photoallergic reactions can be appreciably shortened by placing the patient in a dark room for several days or weeks (see p. 00)

Phenergan,® while being a potent photosensitizer after topical application, in the editors' experience has not caused photosensitization after oral administration in many hundreds of subjects.—Eds.]

Skin Eruptions Following Use of Diamox® (acetazoleamide) a nonmercurial oral diuretic of sulfonamide derivation are reported by Maxwell Spring[5] (New York Med. College) Toxic skin eruptions and agranulocytosis have previously been reported

CASE 1.—Woman, 55 hypertensive had right and left ventricular failure. After one week of diamox® therapy an itchy papular eruption appeared on the arms and legs, which became generalized, erythematous and vesicular except for the face. Erythema multiforme bullosum was diagnosed. The drug was discontinued. ACTH and hydrocortisone were given, and the eruption disappeared. Six weeks later the patient took 375 mg diamox® a severe generalized urticaria followed, which also responded to steroid therapy She was subsequently controlled on oral and parenteral mercurial diuretics without further difficulty

CASE 2.—Man, 32, in congestive failure associated with coronary sclerosis, could not be controlled with mercurials. Diamox® produced a mild papular eruption on the arms and legs which disappeared after the drug was discontinued. Two months later diamox® therapy was resumed the papular eruption reappeared on the chest, face and neck, but disappeared spontaneously though the drug was continued.

Any drug can produce a hypersensitivity reaction in a susceptible person particularly if it is related to a known sensitizer such as sulfonamides Neither patient was known to be sensitive to sulfonamides but both reacted to relatively small doses of diamox,® indicating the allergic nature of the eruptions.

► [For further comment see the leading article this YEAR BOOK.—Eds.]

Thrombocytes and Serology in Cutaneous Drug Allergies were studied by H Storck and R Hoigné[6] (Univ of Zurich) Three methods may be used to determine allergens in cutaneous drug hypersensitivity and other skin allergies

1 Thrombocyte in vivo test (or thrombopenic index test) —In the morning resting and fasting patients are exposed to small quantities of allergen (several intracutaneous allergen wheals and minimal amounts of allergen orally or by injection) In cases of sensitization thrombocytes of the peripheral blood are reduced within 1½ hours by 15% of the initial value. This test proved of value in all groups of allergen

(5) Ann. Allergy 14 41-43 Jan Feb 1956
(6) Dermatologica 112 405-418, Apr June 1956.

(inhalants foods and drugs) and independent of pathologi cally reacting shock organs (skin respiratory system and digestive tract)

2 *Thrombocyte n vitro test*—On the addition of allergen dilutions to oxalated blood, smears show a slight agglutina tion of thrombocytes when the dilution is optimal and platelets are exactly counted and judged. This agglutination depends on two thermolabile serum factors a specific factor I which is dialyzable through a cellophane membrane, and an unspecific nondialyzable factor II found in nonsensitized control persons and in animal serums (guinea pigs, cattle and horses) Since the reaction is positive with thrombocytes of sensitized and nonsensitized persons, thrombocytes were assumed to be a passive ind cator In vitro and in vivo tests generally run parallel.

3 *Serologic-nephelometric method*—In plasma as well as in serum of sens tized persons a slight turbidity develops on addition f allergen within an optimal range of dilutions In this eaction, whi h is also independent of allergen groups and shock organs, serum factors I and II a e also responsible whereas thrombocytes do not participate but serve as in dicators only s ce esults are the same in plasma and in serum

These methods were used n 89 cases of urticaria, drug eruptions and eczematous conditions In 42 cases of urt caria ca sed by drugs the allergen was found by the thrombocyte in test 20 times (with 3 failures) the thrombocyte in tro test 4 times, the nephelometric method 19 times (no f ilur) nd th intracutaneo s test only 19 times (32 fail ures) In 24 cases of drug eruption (fixed, maculopapular pityria form and mult form exanthemas) the allergen was ascertained by the thrombocyte in itro test once, the nephel ometric method 13 times (no failure) and the ntracutaneous test nly 3 t mes (11 failures) In 23 case of eczematous con d t n (contact dermatitis, seborrheic dermatitis, endoge nou ec ema nd dysh dros form eczematous eruptions) the llergen w dent fied by the thrombocyte n vi o test 17 t mes (f lures) th thrombocyte in vitro test twice the eph lometric method 13 times (1 failur n a case of contact derm tit) and by patch testing 10 times (11 fa lures, par t cularly in seborrheic and endogenous types)

It is concluded that in urt caria, drug exanthema and ec

zema the thrombocyte tests and the nephelometric method are valuable additions to dermatologic test methods for specific diagnosis in allergic diseases and occasionally even superior to cutaneous tests Further investigations may reveal whether positive nephelometric and negative cutaneous tests in exanthemas and eczematous conditions point to the skin as not being the shock organ.

Diffuse Hair Loss Associated with Selenium (Selsun®) Sulfide Shampoo was observed in six women by Ralph W Grover[7] (Floral Park N Y) All women had used the shampoo at one to four week intervals for varying periods. It was used from 3 to 10 weeks by 4 2 years by one and 3 years by another Hair loss could not be correlated with administration of any other local or systemic medication and an attempt was made to exclude all other possible causes. It was noted in all that hair loss stopped within a week or two after use of the shampoo was discontinued

An analogy is drawn to hair loss in livestock with chronic selenium intoxication It is concluded that falling hair in these women represented a toxic effect of absorption of the selenium ion and caution is urged in the use of shampoos containing this substance

► [To our knowledge this is the only such report to appear in the literature. In only one instance, and here again a woman, have we seen loss of scalp hair associated chronologically with the use of selsun® suspension The loss did not stop, however when its use was discontinued and it was not possible to establish an etiologic relationship —Eds.]

Resorcin Poisoning is described by A A Cunningham[8] (Kingston England) in the following patient

Boy aged 7 weeks had green slimy bowel movements followed by marked inflammation of the skin of the buttocks, scrotum and neighboring parts. After several treatments failed to clear the rash, resorcin ointment was administered four times. This led to malaise lips, eyelids and skin became deep blue with a yellowish cast.

On examination the child was severely ill with dusky gray cyanosis and rapid respirations. An extensive dermatitis covered the whole diaper area, having a purplish color like the rest of the skin and mucous membranes. The shaft of the penis was edematous. A maculopapular eruption was scattered over the lower buttocks, arms and forearms. The urine contained blood. The hematologic findings indicated hemolytic anemia.

On treatment with calamine lotion and penicillin parenterally the patient improved slowly while the papular eruptions spread.

(7) J.A.M.A. 160 1397 1398 Apr 21 1956
(8) Arch. Dis. Childhood 31 173-176 June, 1956.

After month of supportive treatment, the skin of the trunk had almost completely desquamated apart from a few resistant scaly areas. The diaper area healed and anemia subsided.

This patient illustrates the danger of using resorcin even in the weakest lotion or ointment, on the tender skin of babies and young children with diaper rash, eczema or other eruptions. Absorption may be intense and lethal where the skin is broken, but the ointment may be absorbed and produce serious effects in sensitive subjects, even when the skin is almost intact.

► [The *British Pharmacopoeia* unguentum resorcin contains 12.5% resorcin in base of glycerin, wool fat and soft paraffin. Indeed this is an enormously high concentration of this phenolic compound to apply to large body surfaces, and particularly highly inflamed areas of infants and children. Our own experience, and that of many dermatologists before us, has shown that topical preparations containing resorcin in concentrations of 2 to 3% used over relatively large body areas or on limited areas in adults in concentrations up to 5% are safe. Whenever large body areas are covered, urinalyses should be done at regular intervals for phenolic compounds. Moreover the use of resorcin in infants and young children should be closely supervised and restricted. With this type of precaution, in our experience no instances of resorcin toxicity have been encountered. —Eds.]

4 MISCELLANEOUS DERMATOSES

Sclerolichenoid and Sclerovitiliginous Lesions in Cutaneous Porphyria of Adults. Characteristic clinical signs of cutaneous porphyria of adults mainly include bullous eruptions of exposed skin areas, pinkish or whitish scars secondary to bullae or traumatic excoriation and transitory microcysts. Hyperpigmentation and hypertrichosis may occur. Rose colored or brownish red urine requires examination for uroporphyrin I and III.

M. Bolgert, J. Canet and J. Lépine[a] (Paris) describe sclerolichenoid and sclerovitiliginous lesions in five patients with cutaneous porphyria without abdominal or neurologic symptoms. Situated on the nape, face, retroauricular region, neck and upper chest, these lesions showed anomalies of color and consistency. These more or less well defined, smaller or larger plaques were bright red or bluish red, sometimes white and often showing pigment spots. These were macular like ephelides or reticular and caused the vitiliginous

[a] Ann. dermat. et syph. 8: 141-1 5, Mar.-Apr. 34.

appearance of many lesions Some lesions appeared sclerodermiform others had a slightly scaly surface with exaggerated markings and lichenification Pruritus was absent. Some of the scleroderma like lesions were lusterless, dull, whitish and markedly thinned i e. scleroatrophic. In one case retroauricular lesions were scleroatrophic but showed marked redness a rather rare concurrence. Scleroderma like changes in chronic cutaneous porphyria have been clinically and histologically described by Brunsting who found increased melanin and round amorphous masses of abnormal collagen with altered elastic fibers in the dermis

Porphyria Cutanea Tarda Simulating Dermatitis Factitia. Porphyria cutanea tarda is usually benign of insidious onset in older patients and with few or no systemic symptoms except mild hepatic insufficiency In most patients signs of the disease are limited to the skin and porphobilinogen is absent although large amounts of uroporphyrin and coproporphyrin are excreted in the urine and feces. Occasionally instances occur in which features of classic intermittent porphyria may be combined with porphyria cutanea tarda, the so-called mixed type The disease recurs intermittently for years with an unusual combination of symptoms as seen in the case reported by Harold O Perry and Louis A Brunsting[1] (Mayo Clinic and Found.)

Woman, 53 was hospitalized for evaluation of a bullous skin eruption that had been present recurrently for 8-10 years and was associated with nausea, vomiting and probable jaundice On admission she had chills, temperature of 103 F nausea, vomiting and generalized aching Previously she was considered to have had a psychoneurosis with self induced skin lesions.

The skin of exposed areas of the body was mahogany colored, accounted for by suffusion and hyperpigmentation of these tissues. The sharpness of the nose was accentuated which helped produce a sclerodermoid facial appearance. Marked hirsutism was present in the beard area, extending to the malar prominences. Bullae a few millimeters to several centimeters in diameter were scattered over the face, forearms and hands, and lower part of the legs and feet, being most numerous on the upper extremities.

The contents of some bullae were hemorrhagic, unlike the clear contents in most of the lesions. Ruptured bullae had been replaced by dark brown almost black, thick, adherent crusts. Uniform-sized, hypopigmented superficial, atrophic scars were visible over the cheeks and upper extremities. Analysis of the contents of a bulla

(1) A M A. Arch. Dermat. 74 195-201 August, 1956.

revealed coproporphyrin and protoporphyrin. There was a trong primary fluorescence of the fluid with ultraviolet light.

The patient had spiking daily temperature and hoarseness progressing to aphonia. The slight jaundice, noted on admission, deepened and she appeared moribund.

On restoration of the electrolyte balance and on oxytetracycline therapy there was dramatic improvement. However new "blisters appeared. The ruptured bullae had resulted in irregular crusted ulcerations that measured up to 10 cm. in greatest diameter. Close inspection revealed that the ulcerations on the dorsum of the hands were so deep that elevating a free margin of some crusts exposed the extensor tendons of the fingers. The crusts were escharotic being black and leathery with little purulent material. Si months later scarring from the ulcerations had resulted in some contractural deformities of the fingers.

Absence of porphobilinogen in the urine and presence of toporphyri m urine and feces and of protoporphyrin in the feces, established the patient s disease as porphyria cutanea tarda

► [Note that this patient as thought to have psychoneurosis and self inflicted lesions until the authors established the diagnosis of porphyria cutanea tarda —Eds]

Familial Polymorphous Light Eruption is extremely rare. Light eruptions of the erythematou type n three members of one family and n one of two members of another family is described by A. Wiskemann[2] (Un of Hamburg) as one of many forms of polymorphous l ght eruption This type is haracterized by (1) redness and sw lling of the kin after exposure t l ght but no eczematous reaction (2) pruritus at t m s, but mainly burning sensations (3) with complete protect on f om l ght d sappearance within a f w hours or days without res d es (4) onset i earliest childhood (5) eliciting range f th pectrum between 31 and 615 mμ, with opt mal el citation by is bl l ght (6) no direct pig mentation and (7) hereditary with so far undeterm ned tran m on

The elic t g range of the pectrum d ffers from that of nonf m lial light eruption by l son of con iderable port on f the ble pectrum Inab l ty to form direct pig ment t on occurs n most polymorphou l ght eruption In th uthor patient ligl t urticaria could be excluded be cause t eact f ster nd stronger to far less intensi e radi tion ppea f r the first time n middle-aged persons,

[2] Arch klin. exper Dermat. 203 321 330 1956

disappears quicker and is not elicited by visible light of wave length greater than 500 mμ

According to some observations an absorption band at 500 mμ in the urine may be seen in all polymorphous light eruptions during exacerbations Two of the patients excreted such substances in the urine without having had exposure to light before the examination

Polymorphic Light Eruptions Relation to Ultraviolet Light Intensity and Hours of Sunshine. At wavelengths of 2,500-4 000 A ultraviolet rays penetrate the skin to depths increasing with the wavelengths As a result of skin absorption only about 5% penetrates to a depth of 0 5 mm. Only absorbed rays can produce biologic effects

H Brodthagen and J V Christiansen[3] (Finsen Inst., Copenhagen) studied the correlation between polymorphic light eruptions and light intensity They followed the course of polymorphic light eruptions in 58 patients who were treated prophylactically or curatively with chloroquine diphosphate. Average age was 43 years and average duration of the disorder 15 years Forty patients showed the eruption for the first time 45 aggravations were observed in 29 patients during treatment and relapses occurred in 11 patients one to seven weeks after discontinuation of treatment. Outbreaks occurred mainly during five periods 2d 3d week, 8th-9th week 14th 18th week 20th 23d week and 26th 28th week. The snow that covered the ground during the first two weeks strongly reflected the ultraviolet rays.

Eruptions and aggravations followed closely the periods of greatest light intensity It is suggested that polymorphic light eruptions are due more to *increases* in the intensity of ultraviolet rays than to the *absolute* intensity

► [Most ultraviolet, in particular that in the region of 3,000 A, is almost wholly absorbed within the first 100 μ of tissue.—Eds.]

Diagnosis of Chronic Polymorphous Light Eruptions is discussed by Arthur Wiskemann (Univ of Hamburg) Its clinical appearance is multiform and includes papular and eczematous light eruptions (Hutchinson s summer prurigo Willan s eczema solare) but also transitory erythematous swellings caused by light and lesions strongly resembling lupus erythematosus Diagnosis is usually supported by the

(3) Brit. J Dermat. 68:261 263, July Aug., 1956.
(4) Hautarzt 7 162 163, April, 1956.

patient's history, i.e. there are recurrences in spring and no manifestations in winter. The eruptions are localized on the face and exposed parts, but it may be difficult to differentiate between this condition and dermatitis, neurodermatitis, seborrheic dermatitis and lupus erythematosus, chiefly because light hypersensitivity and other examinations are valuable only under certain conditions and with limitations. For instance, Kimmig's "light band," produced by substances extracted from urine which cause absorption between 480 and 520 mμ of the spectrum, is seen not only in light dermatoses but may be absent in polymorphous light eruption if there has been no exposure to light before examination of the urine. Erythema threshold values under mercury vapor lamp spectrum (which is rather poor in UVA and visible light) are not lowered beyond individual variations when UVB does not participate in eliciting the light eruption. Flare-up of the lesions produced by nonfiltered sunlight is not necessarily proof of such an eruption, because dermatitis and eczema may get worse after light exposure. Lupus erythematosus can be provoked.

To understand the seldom used abbreviations UVA and UVB it should be remembered that the ultraviolet spectrum of optic radiation has been subdivided with reference to biologic effects in (1) UVA (400-315 mμ) with deep-reaching action, e.g. curative in lupus, (2) UVB (315-280 mμ) with an erythema producing effect and (3) UVC (280 mμ) with germicidal effects.

The clinical diagnosis of polymorphous light eruption could be confirmed by light tests on apparently normal skin of the back and thighs. For testing hypersensitivity to UVB the spectrum of the mercury vapor lamp was used, the lines 270-302 mμ and 312 mμ of which were isolated by proper filter. If the erythema thresholds thus produced were markedly below the lowest found in control persons, hypersensitivity to UVB could be assumed. Correspondingly hypersensitivity to UVA was tested by exposure to sunlight or an Osram Xenon lamp (type XBF 6000), the spectral parts <320 mμ of which were filtered away by Schott absorption filter (2 mm). In every one of 21 cases a reaction was noted after three fourths of an average erythema threshold dose, elicited with 320 mμ. Eighteen of the confirmed light erup-

disappears quicker and is not elicited by visible light of wave length greater than 500 mμ.

According to some observations, an absorption band at 500 mμ in the urine may be seen in all polymorphous light eruptions during exacerbations. Two of the patients excreted such substances in the urine without having had exposure to light before the examination

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(4) Hautarzt 7 163 163, April, 1956.

There were two small submucous hematomas in the left nasal cavity.

Histologic study revealed smaller vessels of the corium surrounded by somewhat loosened, homogeneous connective tissue with moderate histiocyte fibroblast infiltrates. Berlin blue-stained sections showed considerable hemosiderin deposits in histiocytes and sweat glands. In McManus-stained sections, the hemosiderin-loaded histiocytes were strongly PAS-positive some capillaries and arterioles displayed spotty pinkish, homogeneous serum precipitates in the lumen.

Because of the hepatosplenomegaly dysproteinemia (with moderate hyperprotein and excessive gamma globulin values) positive Coombs test and a peculiar hemorrhagic diathesis involving skin and mucosa, was classified as purpura hyperglobulinemia. The



Fig. 1. Purpura hyperglobulinemica on upper arm and forearm. (Courtesy of Korting, G. W. and Rehm, G. Arch. klin. exper. Dermat. 20 449-463 956.)

Coombs test is based on th h pothes that certain blocking antibodies are glob l ns that can be demonstrated by anti-human globulin serum that agglutinates erythrocytes. Not only e gamma globulin attached to red blood cell but they also were excessively increased in the authors case Th Coombs test is pos tive n 83% of patients w th acqui ed hem lytic anemia The patients also show a high sediment tion rate hepatosplenomegaly hyperchromic hemogr m w th hypersideremia, increased blood reticulocytes nd redu ed total cholesterols, all of which were found in K rt ng and R ehm s patient. The pos t e Coombs test, labo t ry findings and occurrence of considerable hemo- len depos ts indicat ymptomatic hemolyt c anemia and purp ra pect ely whereas hi tologic find ngs of precipi t t l k h mogeneous protein n th lumen of small, oth rw se unaltered capillaries and rt rioles ind cate dys- mia Th llustrates the complexity of the patho-

tions showed indirect pigmentation i.e., formation of new pigment under UVB in contrast to direct or instant pigmentation and oxidative darkening of colorless propigment to melanin under UVA. Only 12 of 90 controls with normal skin did not show direct pigmentation.

Light testing of clinically normal skin by a sunlight or Xenon lamp the spectral parts <320 mμ of which are filtered away together with determination of erythema thresholds under unfiltered mercury vapor lamp are recommended to confirm the clinical diagnosis of light eruption.

Purpura Hyperglobulinemia with Positive Coombs Test. G. W. Korting and G. Brehm[3] (Univ. of Tubingen) report a case.

Man 29 noticed swelling of the legs and nasal and gingival hemorrhages beginning in March 1955. In May 1955 examination showed hepatosplenomegaly moderate anemia and leukopenia, and a blood sedimentation rate of 100/120. In July 1955 examination showed positive serum lability hyperbilirubinemia, hyperglobulinemia (gamma globulins 42.8%) and low thrombocyte values (83, 600). On hospitalization (October 1956) hepatosplenomegaly pretibial edema indolent axillary inguinal and femoral lymphadenitis, and gynecomastia of the right side were evident. Laboratory tests showed hemoglobin 80% red blood cells 2,930 000 color index 1.3 white blood cells 3,800 with 2% basophils, 2% eosinophils, 2% staff cells 70% segmented cells 21% lymphocytes, 3% monocytes and 33.3% reticulocytes anisocytosis polychromasia. Blood sedimentation rate was 125/128. Blood chemistry studies revealed 2.05 mg./100 ml. bilirubin (direct 0.48 mg and indirect 0.57 mg.) 104.7 mg cholesterol and 183 μg./100 ml serum iron. Results of serum tests were thymol turbidity 4+ Weltmann coagulation band 1 9 Takata reaction 1 9 cadmium sulfate test 2+ and formol gel test 4+ (strikingly fast formation of whitish yellow gel). Thrombocytes numbered 158,200. Coagulation and reaction times were normal and prothrombin time was 15 seconds (90%). Osmotic resistance study showed beginning hemolysis with 0.42% NaCl. Coombs test, both direct and indirect, was positive. The Rumpel Leede phenomenon was strongly positive. Marked light sensitivity was present.

The skin showed extensive involvement, particularly of the flanks, abdomen and limbs (flexor more than extensor surfaces). The eruption consisted of densely disseminated partly linear pinpoint to pinhead sized red hemorrhages (Fig. 14) particularly on the legs, where numerous pigmentations (hemosiderin) were apparent. On the chest and lateral aspects of the upper arms were a few penny sized spider like telangiectases. Small red pointlike hemorrhages were seen on both hard and soft palates.

(3) Arch. klin. u. exper. Dermat. 202 449-465 1 '56.

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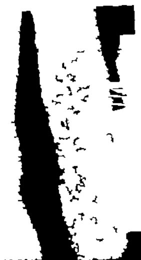


Fig 14.—Purpura hyperglobulinemica on upper arm and forearm (Courtesy of Kortnet, G W and Brehm, G Arch. Klin exper Dermat 203 449 463, 956)

Coombs test i based on the hypothes that certain block ng antibodies are globulins that can be demonstrated b anti-human globulin serum that aggl tinates erythrocytes Not only are gamma globulins atta hed to ed blood cells but they also were excessively increased in the authors case The Coombs test s positive in 83% of patients with cquired hemolytic anemias The patients also show a high sedimentation rat hepatosplenomegaly hyperch om c hemogram with hypersideremia increased blood reticulocytes nd reduced total cholesterols all of which were found in K rt ng and Brehm s patient. The pos ti e Coombs test, laboratory fi dings and occurrence of considerable hemoderin depos ts ind c te symptomatic hemolytic anemia and purpura espectively wherea histologic findings of p ecipi t t lk homogeneous protein in th lumen of small, otherw se unaltered capillaries and arterioles ndicate dysp t inemia Th llustrates the complexity of the patho-

logic process in hyperglobulinemic purpura which, according to Waldenstrom may result from reduced capillary resistance due to the presence of pathologic proteins.

► [An increasing number of these cases is now being reported, indicating that they are probably not quite as rare as was thought after Waldenström's publication (Schweiz. med. Wchnschr 78:927 1948).—Eds.]

Disseminated Pruriginous Angiodermatitis "Eczematid-Like Purpura" (Doucas and Kapetanakis) Itching Purpura" (Loewenthal) was studied in 20 cases by Augusto M Casalá and Santiago J Mosto[6] (Buenos Aires) Six patients were women and most were aged 30-55 years. The three youngest were aged 5 14 and 22 and the oldest 78 years. Most tended to obesity Three patients had had previous injections of vitamin B_{12}.

Constant characteristic symptoms were (1) acute onset with subacute progression (2) punctiform purpura simulating Schamberg's dermatosis (3) localization beginning on the legs with dissemination to the thighs, trunk and upper extremities more severe lesions in large creases face, palms and soles generally spared (4) residual brownish yellow pigmentation (5) pruritus of variable degree (6) histologic appearance analogous to that of progressive pigmentary dermatosis (7) laboratory findings normal tourniquet test positive. Secondary characteristics of the disease were (1) predilection for males (3 1) especially those of pyknic habitus (2) seasonal appearance (spring-summer) (3) papular lesions similar to those in Gougerot and Blum's dermatitis (4) pityroid desquamation simulating eczematid (5) lichenification diffuse or circumscribed (6) arciform distribution in cords or plaques with islets of healthy skin similar to some types of reticulosis (7) atrophic parapsoriasiform appearance.

Course of the disease was three to six months although it may be prolonged by new lesions to one to two years. Most severe cases were of longest duration Most patients studied were treated with rutin vitamins C and K antihistamines and locally with aqueous pastes which favorably influenced progress of the disease Recently better results have been obtained with an oxidized derivative of epinephrine the monosemicarbazone of adrenochrome administered orally

► [It is encouraging that after many years of emphasis on the morpho-

(6) Arch. argent. dermat. 5 209-212, September 1955.

logic aspects of purpuric eruptions, especially of the legs, we are now learning more about the mechanisms producing these eruptions. Among pertinent references which indicate this healthy change are those of Wintrobe and Buell (Bull Johns Hopkins Hosp. 52:156, 1933) and Lerner and Watson (Am. J. Sc. 214:410, 1947) on purpura associated with cryoglobulins Waldenstrom on purpura associated with hyperglobulinemia (Schweiz med. Wchnschr 78:927, 1948) and Gardner and Diamond on purpura associated with autosensitization to red blood cells in women (Blood 10:675, 1955) —Eds.]

Dermatologic Manifestations Associated with Cryoglobulinemia are described in two patients by Mauri Feldaker Harold O Perry and David G Hanlon (Mayo Clinic and Found.) Cryoglobulinemia signifies the presence in the blood of a group of proteins which precipitate or gel from cooled serum. It may occur symptomatically in multiple myeloma, kala-azar malignant lymphomas and leukemias, periarteritis nodosa, bacterial endocarditis, septicemia and liver cirrhosis. The commonest associated dermatologic manifestations are Raynaud's phenomenon purpura, tendency toward mucosal bleeding urticaria, digital gangrene, ulcerations, and various manifestations of sensitivity to cold. Two cases of essential cryoglobulinemia are reported.

Case 1.—Man, 58, had had visual difficulty from uveitis and secondary glaucoma for several years. Tiny nodules were noted on the forehead, extremities and trunk. Some grew peripherally with central clearing and atrophy and were yellowish, painless and asymptomatic, with occasional scaling black discoloration and gangrene in the center Microscopic section showed features of sarcoid structure. Clinically the plaques on the legs suggested necrobiosis lipoidica, and those on the body sarcoid. He had noted intolerance to cold and peripheral vascular instability Significant in the extensive laboratory examination was presence of cryoglobulin, 1.5 Gm./100 cc plasma. Treatment, including empiric use of nitrogen mustard, was relatively ineffectual and primarily supportive and symptomatic Large areas of ulceration developed and finally subsided and cleared entirely only to recur At last word, he had purpuric ed spots over the body especially the face he had little strength, was underweight and tired easil

Case —Woman, 38, had had edema and polyarthritis of the knees hands and ankles with macular purpuric eruption on the ankles After six weeks, the purpura spread all over the lower extremities She had some associated urticaria, but no history of allergy Lesions were annular and clear in the center with no evidence of atrophy She was anemic, with an erythrocyte count of 3,310,000 Cryoglobulin was 1.71 Gm./100 cc serum and total protein 8.37 Gm./100 cc. Treatment was primarily rest, elevation of extremities and elastic supportive bandages on the legs when walk

A.M.A. Arch. Dermat. 73:125- 3, April, 1956.

ing Common allergenic foods such as eggs, chocolate pork and various fruits and vegetables were eliminated. After 10 days of hospitalization response was good and about 90% of purpura had subsided.

Dermatologic manifestations in these patients are consistent with those found in cryoglobulinemia, although it is speculative that cryoglobulins actually cause these symptoms Clinically and histologically findings in the first patient resembled those Miescher noted as granulomatosis disciformis chronica et progressiva " although ulceration was not reported Cryoglobulinemia should be considered in patients with cold sensitivity who show Raynaud s phenomenon purpura or other bleeding tendencies, urticaria and ulceration of the lower extremities

► [The differential diagnosis of various types of hypersensitivity to cold and their dermatologic manifestations are also discussed by Griem and Rothman in *Allergic Dermatoses Due to Physical Agents* (New York New York University Press, 1956) —Eds.]

Unusual Skin Lesions Associated with Thrombosis of Subclavian Artery are reported by M H Samitz and Samuel Lisker[8] (Philadelphia)

Man 53 had painful tips of the index and little fingers of the left hand. About a month before some pieces of cement had adhered to the finger tips of the left hand. Steel wool was used to remove the caked cement. About a week later throbbing pains in the finger tips began which he attributed to the steel wool He also noticed cracking of the finger tip skin Pain became continuous and was intensified by Epsom salt soaks The skin of the involved fingers appeared raw The tip of the index finger was incised and some dead tissue debrided. Antibiotics, given also topically did not help. The condition became worse, the pain unbearable.

On examination the left hand was deeply erythematous, and marked hyperhidrosis of the palmar area was present. The tips of the index and little fingers were edematous and tender a cyanotic to cadaveric color change was present and the skin showed fissuring and ulceration that appeared almost gangrenous. The left radial pulse was nearly imperceptible, whereas the right radial pulse was bounding Blood pressure in the right arm was 130/70 mm. Hg and in the left arm 80/0 The left subclavian artery could not be found and the left brachial artery was barely perceptible. The left common carotid artery was normal on palpation.

A left cervical sympathetic ganglion block was performed using the anterior approach Shortly after a Horner syndrome appeared and sweating of the left half of the face and left hand ceased. Pain in the fingers was considerably less. Next day another block was performed. The ulcerated fingers became warmer and much less

(8) J A M A 161 725-726, June 23 1956.

tender The pallor of the finger-tips was slowly replaced by faint pink color A heavy cotton batting mitten was placed over the hand. Dibenzyline,* 10 mg twice daily seemed to prolong relief. After the second block, there was definite improvement in the oscillometric indexes, particularly regarding pressure at which they were obtained

Six days later another cervical block was done. This was also effective objectively and at this time tips of the involved fingers ere pink and almost as warm as the others. The little finger was completely healed and painless. The index finger was painless and could be flexed and extended, and the ulcer was healing rapidly. Seven more cervical sympathetic ganglion blocks were performed at fiv t seven day intervals. The ulcer on the index finger healed completely

► [An instructive, excellent case report of very unusual syndrome and its management.—Eds.]

Melanoma-Simulating Nodules Due to Capillary Aneurysms wer observed by Ervin Epstein, Frederick G Novy Jr Richard A. Skahen and Max E. Krause* (Oakland, Calif) in six patients aged 31 59 The nodules were facial in fi e a d rapidly enlarging in three. No pat ent had had a pre-xisting evus

Microscop cally the lesion consisted of a dilated ascular hannel lying immediately beneath the epidermis The chan nel was of a capillary structure, i.e., lined by a single layer of endothelial cell and surrounded by a few concentric layers of ollagenous connective tissue. No muscle fibers or elastic tis ue w seen in the wall The connective tissue surround ng the vascula channel was slightly edematous but other wise not rema kable In one instance, a mall mural throm bus was seen adherent to the vessel wall. A few fibroblasts in the edge f the thrombus indicated ea ly organizat on. Serial section of on lesion indicated that the dilation is essentially pherical d terminates n a small capillary n the upper derm

It d fficult to justify the all too common sacrifice of nor mal kin nd ubcutaneous tissue just because it happens to djoin bla k smooth tumor Actually su h lesions are more ften benign than malignant, a underscored n the list of lesion that may present these features. It ncludes blue ne- u junction ne pigmented basal cell epithelioma, mela notic freckl epithelial nd sebaceous cysts, granuloma pyogenicum glomus tumor hema gioma, hemorrhage fibro-

C forn Med. 81 22 31, July 1954

angioma and angiosarcoma. To this list the authors add capillary aneurysm Growth is common and bleeding may occur in these aneurysms. Metastasis does not occur but it would be possible if unlikely for such a lesion to be multiple. The black color often intensifies as the tumor grows. Ulceration has not been reported

► [To quote the authors "This should not be construed as recommending the minimizing of the black lesion rather it is a plea for the exercise of therapeutic perspective instead of the wanton sacrifice of flesh in benign lesions. We agree that where the clinical diagnosis of malignant melanoma is in doubt, conservative though adequate excision of the entire lesion should be done.—Eds]

Histiocytemia with Cutaneous Manifestations was observed in a patient by Philip D Christensen[1] (Minneapolis)

Man 59 had had recurrent episodes of anorexia, diarrhea, weight loss fever and an eruption which started on the nape. Physical



Fig. 15.—Photograph illustrating extent and distribution of papular lesion (Courtesy of Christensen, P D. A.M.A. Arch. Dermat. 73 582 584 June, 1956.)

examination revealed a chronically ill man with obvious weight loss. An eruption was present on the sides and back of the neck (Fig 15) anterior and posterior axillary folds, scapular regions, ischial tuberosities and medial aspect of the knees, being more pronounced in the first three areas mentioned. The small lesions were irregular red macules, and they preceded the development of larger papular lesions. The larger lesions were violaceous, smooth pap-

(1) A M.A. Arch. Dermat. 73 582 584 June, 1956

ules which tended to be confluent in circular plaques. They were not indurated, and they blanched with pressure. Small lymph nodes were palpable in the left axilla. There was splenomegaly.

Further examinations revealed numerous typical histiocytes in the peripheral blood and bone marrow, normochromic, normocytic anemia, gastric achlorhydria with histamine, elevated sedimentation rate, hyperglobulinemia, 1+ albuminuria, and minimal microscopic hematuria. No pathologic changes were found in liver and lymph node biopsy specimens. Biopsies from all areas of the eruption showed dilated capillaries in the upper corium filled with histiocytes. No other marked changes were found in the skin.

He was given 21,400,000 units of penicillin, 35 Gm. streptomycin and 28.5 Gm. chloramphenicol. The symptoms cleared to a large extent, though the skin eruption remained unchanged.

The etiology of this condition is unknown. The cutaneous eruption is apparently secondary to the histiocytemia, leading to histiocytic thrombi.

* [An addendum to this article states: "Histologic sections of the skin lesions were shown at the Clinical Pathologic Conference held during the 14th Annual Meeting of the American Academy of Dermatology and Syphilology. A diagnosis of angioendothelioma corporis diffusum was suggested by several members of the panel. —Eds.]

Ocular Sarcoidosis. Sarcoid lesions are histologically characterized by aggregates of large pale epithelioid cells and occasional giant cells grouped in nests compressing or displacing normal tissue. There is little or no necrosis or caseation. Eventually the lesions resolve and are replaced by acellular hyaline material, followed by dense fibrosis. At an intermediate stage, granulomatous foci, hyaline tissue and fibrosis may be seen together. Iridocyclitis is the commonest ocular manifestation of sarcoidosis, and while this is usually self-limiting, fibrosis associated with healing may lead to disorganization of the globe and loss of sight.

Among 100 patients with histologically confirmed sarcoidosis, D. Ainslie and D. Geraint James[3] (London) observed eye changes in 28. Bilateral, chronic iridocyclitis was seen in 1? of them had also choroiditis. Although nodules in the iris have often been described as typical of iridocyclitis due to sarcoidosis, they were seen in only two patients.

In 14 of the 28, the following skin changes were seen: erythema nodosum 4, lupus pernio 2, dusky red papules, 4, herpetiform lesions 1, and scars of old injuries in which biopsy revealed sarcoid tissue 3. Sarcoid tissue involving old cut neous scars is common, and such scars may become ed

[3] Brit. M. J. 1:954-957, Apr. 28, 1956.

and livid during exacerbations of the disease. This was noted by three patients during exacerbations of iridocyclitis.

Pulmonary changes occurred in 23—bilateral hilar lymphadenopathy in 9, diffuse mottling of lung fields in 7 and both in 7.

In absence of easily accessible lesions for biopsy, the Kveim test is a simple, safe and specific outpatient technic for providing histologic evidence of active sarcoidosis. It was performed in 19 patients with ocular sarcoidosis and was positive in 15. This rate of 79% is similar to that found in all types of sarcoidosis.

Cortisone or hydrocortisone applied locally is usually effective. Cortisone is generally administered as drops (0.25-1%) or ointment (1%) applied to the conjunctival sac at intervals of 2-12 hours. In severe cases, an initial subconjunctival injection of cortisone or hydrocortisone (5-10 mg.) insures a high concentration in the eye. The dose may be repeated in three to four days, after which topical application is usually sufficient. In all instances of iridocyclitis, a mydriatic should be used with the cortisone therapy.

Erythema Nodosum as Manifestation of Sarcoidosis. Erythema nodosum is a reaction to many infections and drugs. Its cause is often difficult to determine with certainty and the histologic appearance of the skin lesions is usually nonspecific. D. Geraint James, A. D. Thompson and A. Willcox[1] (Middlesex Hosp., London) report data on 7 men and 20 women aged 18-60 in whom there was histologic evidence of sarcoid tissue at the time of erythema nodosum. Tubercle bacilli were not isolated from any patient, although they were sought in biopsy material, sputum and, if necessary, gastric washings. Evidence of sarcoidosis was obtained by biopsy of a lymph node (4 patients), skin (5), liver (4), Kveim test (19) and directly from a skin lesion of erythema nodosum (2).

Lesions of erythema nodosum were characteristic. They were always present on the legs but also occurred on the arms of four patients. They persisted for one to six weeks. Some constitutional disturbance was usual at onset, with pyrexia up to 102 F. for the first few days.

Associated polyarthritis, usually involving knees, ankles,

(1) Lancet 2:218-221, Aug. 4, 1956.

wrists and elbows, was present in 17 (63%) preced ng the erythema nodosum n 11

Bilateral enlargement of hilar lymph nodes, seen on chest rays, was present in 24 enlargement of paratracheal nodes, present in 6, was always unilateral and right s ded. Enlargement persisted for 2 12 months. In five, transient bilateral diffuse parenchymal mottling developed as hilar node en largement subs ded.

The intradermal reaction to old tuberculin, 1 100 was posit in 13 and negative n 14 Red and white cell counts revealed no abnormality but the sedimentation rate was al way ften greatly increased.

Erythema nodosum as a manifestation of sarcoidosis has a fa orable prognosis. Histologic evidence to segregate this group from erythema nodosum due to other causes is mpor ta t

► [The question here is whether these were cases of true erythema nodosum in sarcoidosis or hether the authors wer dealing with nodular lesions of sarcoidosis, resembling erythema nodosum.—Eds.]

Multiple Cutaneous and Subcutaneous Sarcoid-Like Foreign Body Granulomas Report of Case with Parallel Course in Various Sites. Sarcoid-like granuloma elated to an old injury has been reported in 43 instances 6 were attributed to land mine injury Multiple f reign body granulomas were observed by Robert Brandt and Harold Plotnick[4] (Uni of C ncinnati) n th f llowing patient

Man, 28 injured nine year before by a land mine explosion, noticed sudden onset of "bumps on the back of the neck and some swelling in areas of the old war injuries of the left arm and palm On the back of the neck, near the hairline and partly extending int the hairy rea, was herpetiform group of small yellow sh nodules The grouped lesion w about 2 cm. in greatest diamete The individual papule of thi lesion w translucent, mpressible fimd free nd overlaid with telangiecta ia. Diascopic pressure evealed blue to bluish black discoloration dispersed in and between ndi idual elevated lesions The pigment was inter preted pow ler burn residue A biopsy pecimen was taken from th region (ramally and to the left of this lesion, was subcutaneous infilt te about 1 5 cm. in diameter A few scars w th embedded powder mark and some indication of ssociated infiltrate er seen in the midlateral spect of the left m In the web f th (sue between the left thumb and index finger on the palmar surface a an indurated rea. The patient stated that this area involved in the original injury and since then had been tender

Later the papules in the nuchal region became more raised, firmer and brownish. Under diascopy the lesions simulated apple jelly nodules. They remained stationary for two months without treatment. Suddenly the patient noted softening of all lesions and ensuing gradual involution. The subcutaneous infiltrates regressed more than the grouped papular lesions on the neck. Four months later all papular lesions had disappeared and only powder burn residue was visible.

Histologic studies revealed slight hyperkeratosis over an otherwise thin epidermis. The corium, down to the base of the biopsy specimen, contained multiple, various-sized, focally coalescent, tuberculoid granulomas composed of epithelioid cells and scattered multinucleated giant cells. Several asteroid inclusion bodies were identified. There was no evidence of necrosis. Under the polarizing microscope, birefringent crystals were noted in the epithelioid cell reaction.

Whether sarcoid like granuloma arises in response to some specific local factor or to a special general reactivity of the host has been discussed by various investigators. The specific agent may be the important factor e.g. silicon as in this case and beryllium compounds produce this reaction more often than other substances. In the authors patient, the almost spontaneous appearance and disappearance in all involved areas indicates some unknown systemic factor.

Hypodermitis Nodularis Subacuta Migrans in 11 women, aged 22 54 is reported by X. Vilanova and J. Pinol Aguadé[5] (Barcelona). Histories of the 11 revealed recurrent tonsillitis in 8, previous tonsillectomy in 4 and concomitant arthralgia in 3. Onset of the disease was characteristic: cutaneous manifestations appeared 1 20 days after tonsillitis or marked pharyngitis with or without transitory arthralgia. The lesions were first painless or only slightly sensitive doughy rather than indurated subcutaneous nodules mostly situated on the anterolateral aspect of the legs and were not adherent to skin or underlying tissues. They gradually enlarged into often ill defined plaques of 10-20 cm. diameter (Fig 16). These plaques sometimes circinate occasionally had a sclerodermiform consistency in the center which was yellow red or bluish red whereas the peripheral zones of enlargement were mostly bright red. Skin covering the plaques was adherent but the plaques were movable over deep tissues. After one week to three months the plaques gradually disappeared leaving slight hyperpigmentation and transitory

(5) Ann. dermat. et syph. 83 369-404 July Aug. 1956.

scaliness but no scars. During evolution or involution of the plaques, new nodules appeared, prolonging the course of the disease (migrans) Plaques were mostly situated on the legs a d occasionally on the thighs m two patients they were gluteal. Septic foci were seen in three of nine patients (dental granuloma, sinusitis, chronic t nsillitis) otherwise, results of physical examination were negative Laboratory tests showed a slightly raised sedimentation rate hemograms proteinograms, Weltmann coagulation band, Takata Ara test, blood chemistry and blood cultures were negative. In



Fig 14 (Courtesy of Vilanova, X and Piñol Aguadé, J Ann. dermat et syph 83 369-404, July-Aug 1956.)

tracutaneous tuberculin tests (1 10,000) were negative or weakly positi e in four patients.

Histologic examination revealed three main changes (1) subcutaneous capillaritis in nvolved areas, (2) characteristic topographic localization nd composition of infiltrates and (3) collagen changes Subcutaneous capillaritis which also represented the initial lesion was characterized by prolifer ation and swelling of endothelial elements, increase of peri-cytes and narrow ng to obliteration of vascular lumens. These ha ges occurred mainly in interlobular con ecti e t ue nd inner part of fat lobules the dermohypodermic junction wa less in l ed or uninvol ed. Later some capillaries t rted functioni g again others, more damaged,

showed changes of giant cell capillaritis Few were encased in the connective tissue that finally caused sclerosing of the vessels With onset of capillaritis proliferation of pericytes and fixed connective tissue cells occurred later scanty histiocytic lymphocytic infiltrates formed between collagen bundles and fat lobules Among proliferating connective tissue cells lipophages were seen Infiltrates were accompanied or preceded by edema which dissociated collagen fibers already changing their staining affinities and fragmenting

Sulfonamides penicillin streptomycin chloramphenicol, vitamin C salicylates tonsillectomy and removal of the dental granuloma had no therapeutic value a single intravenous injection of nonspecific protein was effective in one patient, but potassium iodide (2 3 Gm./day) produced fast and complete results within a few days in the five patients receiving this treatment This seems to contradict a purely infectious etiology As to the pathogenesis a vascular sensitization to a yet unknown allergen or micro-organism may be hypothecated the sensitization however involving the capillaries of the subcutis and not larger vessels as in erythema nodosum

Differential diagnosis must mainly consider erythema nodosum which with concomitant fever anorexia, sore throat overfatigue pains and joint stiffness shows symmetrical, nonextensive often contusiform lesions Single lesions last but a few days the eruption about three to six weeks Salicylates are promptly effective Erythema nodosum may be idiopathic infectious toxic or caused by drugs Histologic study reveals involvement of larger vessels perivascular infiltrates with numerous polynuclear cells and Miescher granulomas Hypodermitis nodularis subacuta migrans however occurs mostly in adult females there are no acute attacks and only one or two even three nodules appear at a time, which are extensive i e heal in one part and extend in another This fact with the appearance of successive new lesions causes the prolonged subacute and migratory character of the condition. General health is affected little or not at all treatment with potassium iodide is highly effective. Histologically hypodermal capillaritis subcutaneous histiocytic lymphocytic infiltrates and collagen changes are characteristic. Infiltrates are never dense and contain no polynuclear cells or Miescher s granulomas

In Pfeiffer Weber-Christian syndrome, nodules slowly appear in the skin of the l mbs and abdomen, with no prodromes and little or no disturbance of general health. Lesions are small or very large developing into large plaques occasionally liquefying and ulcerat ng eventually healing and lea ng a entral depression, hyper or depigmentation and, on the scalp circumscribed loss of hair behind. In some cases, in olvement of nternal organs and even death hav been recorded. The histologic appearance is that of panniculitis with steatonecrosis, showing infiltration of ad pose tissue with polynuclear and lipophagic cells, formation of lipophagic granulomas and eventual substitution of adipose tissues by fibrosis.

Panniculitis of Rothman and Makai occurs in infants and ung hildren nodular vascul tis, also called erythema induratum mplex nontuberculosum or hypodermite nodulaire (Gougerot) has the l nical appearance of erythema induratum (Bazin)

* [The question arises as to the mechanism by which iodine exerted its beneficial effects in all five cases in which it was given Could it have been in the thyroid? In that event thyroid dysfunction might have played role in these cases N data regarding thyroid activity are given in the original article —Eds]

Lupus Erythematosus Profundus (Kaposi Irgang) Report of Case Including Comparative Study of Histopathology with That of Chronic Discoid Lupus Erythematosus. The iew of Pautri r that lupu erythematosus profundu is merely l pu rythematosu of the face and scalp with subcutaneou tuberculids or sarcoid in other part of the ntegument d sputed by Frances Pascher Charles F S m nd Nathan Pensky[3] (New York Uni Post-Grad. Med School and Sk n nd Cancer U n t) on the basis of re ew of hi tologic pecimen f unequ ocal cases of chronic discoid lupus erythematosus w th attention to th deeper tructures.

Of 213 histologic pecimen of chron c discoid lupus erythematosus 100 ncluded th subcutaneous fat. Among these th dermohypodermal z ne and fat were spared n 72 Among the rest a parse reaction in the deep corium and fat wa found in 20 m ld reaction in 5 and a moderate reaction n 3 The changes in the deep corium and subcutaneous fat w r non pecific imulat g the picture of pannicul t s nodula ascult and erythema nodosum Th pathognomon fea

[3] J Invest. Dermat. 25 347 362, November 1955.

showed changes of giant cell capillaritis. Few were encased in the connective tissue that finally caused sclerosing of the vessels. With onset of capillaritis proliferation of pericytes and fixed connective tissue cells occurred; later scanty histiocytic lymphocytic infiltrates formed between collagen bundles and fat lobules. Among proliferating connective tissue cells lipophages were seen. Infiltrates were accompanied or preceded by edema which dissociated collagen fibers already changing their staining affinities and fragmenting.

Sulfonamides, penicillin, streptomycin, chloramphenicol, vitamin C, salicylates, tonsillectomy and removal of the dental granuloma had no therapeutic value; a single intravenous injection of nonspecific protein was effective in one patient, but potassium iodide (2 3 Gm./day) produced fast and complete results within a few days in the five patients receiving this treatment. This seems to contradict a purely infectious etiology. As to the pathogenesis a vascular sensitization to a yet unknown allergen or micro-organism may be hypothecated, the sensitization however involving the capillaries of the subcutis and not larger vessels as in erythema nodosum.

Differential diagnosis must mainly consider erythema nodosum which, with concomitant fever, anorexia, sore throat, overfatigue, pains and joint stiffness, shows symmetrical, nonextensive, often contusiform lesions. Single lesions last but a few days, the eruption about three to six weeks. Salicylates are promptly effective. Erythema nodosum may be idiopathic, infectious, toxic or caused by drugs. Histologic study reveals involvement of larger vessels, perivascular infiltrates with numerous polynuclear cells and Miescher granulomas. Hypodermitis nodularis subacuta migrans however occurs mostly in adult females; there are no acute attacks and only one or two, even three, nodules appear at a time which are extensive, i.e., heal in one part and extend in another. This fact with the appearance of successive new lesions causes the prolonged subacute and migratory character of the condition. General health is affected little or not at all; treatment with potassium iodide is highly effective. Histologically, hypodermal capillaritis, subcutaneous histiocytic lymphocytic infiltrates and collagen changes are characteristic. Infiltrates are never dense and contain no polynuclear cells or Miescher's granulomas.

In Pfeiffer-Weber-Christian syndrome nodules slowly appear in the skin of the limbs and abdomen, with no prodromes and little or no disturbance of general health. Lesions are small or very large, developing into large plaques, occasionally liquefying and ulcerating, eventually healing and leaving a central depression, hyper- or depigmentation and, on the scalp, circumscribed loss of hair behind. In some cases involvement of internal organs and even death have been recorded. The histologic appearance is that of panniculitis with steatonecrosis, showing infiltration of adipose tissue with polynuclear and lipophagic cells, formation of lipophagic granulomas and eventual substitution of adipose tissues by fibrosis.

Panniculitis of Rothman and Makai occurs in infants and young children. Nodular vasculitis, also called erythema induratum simplex nontuberculosum or hypodermite nodulaire (Gougerot), has the clinical appearance of erythema induratum (Bazin).

► [The question arises as to the mechanism by which iodine exerted its beneficial effects in all five cases in which it was given. Could it have been via the thyroid? In that event thyroid dysfunction might have played a role in these cases. No data regarding thyroid activity are given in the original article.—Eds.]

Lupus Erythematosus Profundus (Kaposi-Irgang): Report of Case Including Comparative Study of Histopathology with That of Chronic Discoid Lupus Erythematosus. The view of Pautrier that lupus erythematosus profundus is merely lupus erythematosus of the face and scalp with subcutaneous tuberculids or sarcoids in other parts of the integument is disputed by Frances Pascher, Charles F. Sims and Nathan Pensky[6] (New York Univ. Post-Grad. Med. School and Skin and Cancer Unit) on the basis of review of histologic specimens of unequivocal cases of chronic discoid lupus erythematosus, with attention to the deeper structures.

Of 213 histologic specimens of chronic discoid lupus erythematosus 100 included the subcutaneous fat. Among these the dermohypodermal zone and fat were spared in 72. Among the rest a sparse reaction in the deep corium and fat was found in 20, a mild reaction in 5 and a moderate reaction in 3. The changes in the deep corium and subcutaneous fat were nonspecific, simulating the picture of panniculitis, nodular vasculitis and erythema nodosum. The pathognomonic fea

(6) J. Invest. Dermat. 25: 347-352, November, 1956.

tures of lupus erythematosus were in the epidermis and upper half of the corium. Three pertinent facts were gleaned from this investigation: (1) The deep corium and fat may be involved in discoid lupus. (2) The inflammatory reaction is nonspecific and usually not enough to be registered clinically. (3) The deep changes in chronic discoid lupus and lupus erythematosus profundus differ only quantitatively rather than qualitatively.

Woman, 31, had had an "inflamed" lesion for three years on the outer aspect of the left arm. Ten years before, she had had sun-poisoning with blisters; three years earlier she had had febrile episodes with weakness and joint pains and a "drug rash." A deep indurated inflammatory mass, 6 cm. in diameter, was found on the proximal lateral aspect of the left arm. The area was an irregular depressed plaque encircled by an ill defined violaceous red zone, which was somewhat infiltrated. The central portion had adherent scales. Symmetrically distributed over the anterior and lateral aspects of both arms were about 15 subcutaneous nodules, of hazel nut size, with freely movable overlying skin. Laboratory findings were within normal limits except for slight elevation of the sedimentation rate. No L.E. cells were found. Histologic examination revealed a thin epidermis, spotty liquefaction degeneration of the basal cell layer and some follicular plugging. A patchy infiltrate, consisting of small lymphocytes, histiocytes and an occasional polymorphonuclear leukocyte, was most marked in the deep corium and the subcutaneous fat, especially around the vessels and appendages. The lumens of the vessels were narrowed and the walls thickened and edematous in some instances. Collagen in the upper corium was fragmented, and elastorrhexis was shown with Weigert's stain. After an acute febrile episode some two years later, resorption of the lesion of the left arm proceeded slowly as was the case with the nodules, some of which left surface changes typical of discoid lupus erythematosus. The diagnosis of lupus erythematosus profundus was suggested by the unusual degree of inflammation surrounding and underlying the plaque over the left deltoid and the presence of subcutaneous nodules on both arms.

A *sine qua non* for the diagnosis of lupus erythematosus profundus is presence of typical lesions of lupus somewhere on the scalp or body alone or over the subcutaneous lesions. In absence of this, the typical histologic features of the disease in the skin overlying the nodule should be clearly demonstrable. The subcutaneous nodules are characteristically distributed over the face, arms, buttocks or thighs. The lesions are firm, circumscribed, deep-seated, tender and vary from hazel nut to pigeon egg size. They may be resorbed without trace or extend to the overlying skin with develop-

ment of typical discoid lupus erythematosus or healing may be followed by a hollow or retracted scar of varying size and depth.

The histologic findings may be such as described in the authors case or may resemble acute or subacute lupus erythematosus in which the changes are primarily degenerative and destructive, showing fibrinoid degeneration and necrosis of the collagen in the deep cutis and hypodermis, obliterative and destructive changes in the vessel walls and collagenization of the fat. The cellular infiltrate was scant, distributed principally about foci of necrosis. The absence of epithelioid cells in all reports merits emphasis in view of the association of the term sarcoid with these subcutaneous nodules. The case presented seems to support those workers who contend that a variant such as lupus erythematosus profundus (Kaposi-Irgang) exists if it fulfils the clinical and histologic features described.

► [Involvement of the deep cutis and hypodermis to some extent in 20% of cases and to more than a negligible degree in 8% of cases of chronic discoid lupus erythematosus is a new and important finding. It helps to improve our understanding of the relationship between chronic discoid lupus erythematosus and lupus erythematosus profundus.—Eds.]

Electrophoretic Studies in Disseminated and Fixed Lupus Erythematosus were carried out by Luis Baptista, Gunter Hoxter, Lino Vellini and Raul Mungioli[7] (São Paulo, Brazil) in 6 patients with disseminated and 12 with a fixed type of lupus erythematosus. All showed a decline in levels of albumin and beta globulin with an increase in alpha globulin and fibrinogen. The decrease of albumin and beta globulin was more pronounced in disseminated cases whereas the increase of alpha globulin and fibrinogen was equivalent in both forms. An increase of gamma globulin which had been described by other authors was observed only discretely in five cases of the disseminated and in one of the fixed lupus group. The single patient with disseminated lupus who had exceptional hypergammaglobulinemia had lymph-node tuberculosis with positive guinea pig inoculation, exhibiting a pronounced plasmocytosis, besides an increase in fibrinogen. Hyperproteinemia was observed in one disseminated and in four fixed lupus cases. Severity of the disease could not be correlated with gamma globulin levels. Alpha globulin was

7) Am. J. M. Sc. 232:84-92, July 1956.

increased in four of the disseminated and six of the fixed lupus cases

It should be noted that increase of alpha globulin is far more usual than rise in gamma globulin fraction This simultaneous increase of alpha globulin and fibrinogen (in all but one patient) is usually found in mesenchymopathies and seemed more significant than the hypergammaglobulinemia. Also noteworthy was the constant decrease of beta globulin in all the disseminated and most fixed lupus cases this has also been seen in Nicolas Favre disease and leprosy

Lupus Erythematosus Clinical and Hematologic Studies in 77 Cases. R H Marten and E K Blackburn[8] (Royal Infirm Sheffield England) noted abnormalities of the blood in over 50% of 66 chronic discoid cases, 5 of 6 generalized discoid cases, 4 subacute disseminated cases and 1 acute disseminated case The hematologic abnormalities usually described in acute disseminated lupus erythematosus include hypochromic and hemolytic anemias leukopenia granulopenia eosinophilia thrombocytopenia increased erythrocyte sedimentation rate, cold agglutinins a positive direct Coombs test and L.E cells.

Laboratory tests were made in all cases to determine the presence of any of these abnormalities Clinical symptoms were the classic arthralgia, myalgia weight loss fever mucosal involvement in the chronic discoid cases and splenomegaly O Leary s clinical classification of chronic discoid, generalized discoid subacute and acute disseminated lupus erythematosus was used. Generally the hematologic findings were more prominent as the disease became more acute and disseminated There was little unusual in the findings in the acute disseminated and subacute disseminated cases Among the 66 chronic discoid cases a raised sedimentation rate was found in 24 L.E cells in 9 anemia in 4 leukopenia in 5 low platelet count in 2 positive direct Coombs test in 2 and cold agglutinins in 3 In 14 more than one abnormality was present In a few cases the causes may have been associated with abnormalities other than lupus erythematosus Clinical activity roughly paralleled presence of hematologic abnormalities In seven of eight cases the skin lesions remained unaltered or improved during pregnancy irrespective of pres-

(8) A.M A. Arch. Dermat. 73 1 14 January 1956

ence or absence of blood changes. Presence of inactive skin lesions in chronic discoid lupus erythematosus does not necessarily denote inactivity of the disease, however presence of leukopenia or L.E. cells may presage future dissemination of the disease. The average number of L.E. cells in acute and subacute disseminated lupus erythematosus is considerably greater than in the chronic discoid type.

Significance of hematologic abnormalities in chronic discoid cases can be assessed only after prolonged clinical and hematologic follow-up.

▸ [An incidence of over 50% hematologic abnormalities, including 9 cases with L.E. cells in the peripheral blood, among 66 cases of chronic discoid lupus erythematosus is striking and unexpected, as are the finding of 12 cases of arthralgia or arthritis and 3 cases of myalgia among these 66 cases. This raises the question, of course, whether the authors' 66 cases are actually chronic discoid lupus erythematosus.—Ed.]

Histopathology of Cutaneous Lesions in Systemic Lupus Erythematosus was investigated by Michel Prunieras and Hamilton Montgomery[4] (Mayo Clinic and Found.) in 38 cases. It was found that early stages of the cutaneous eruption are not diagnostic, but when a lesion has been present for four weeks histopathologic changes may be considered diagnostic if all previous irritating topical or roentgen therapy has been excluded.

The periodic acid Schiff reaction showed constant changes in the basement membrane accompanied by intense macrophage activity of connective tissue cells. Fibrinoid changes in vessels were less usual than previous reports indicate.

A positive pyridine-resistant reaction to sudan black B was found in five instances, possibly related to early senile changes in connective tissue fibers. With methyl green pyronine stain controlled by ribonuclease and perchloric acid extraction (modified Brachet test) intracellular bodies termed "red bodies" were found. These represented depolymerization of desoxyribonucleic acid in lymphocyte nuclei. These changes were a frequent and nonspecific finding. They apparently occur also in nuclei of connective tissue cells as a possible early stage in formation of "hematoxylin bodies."

Hargraves has stated that loss of chromatin pattern of engulfed nucleic material is the basic criterion of the L.E. phenomenon in blood. This applies also to the red bodies in

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(4) A.M.A. Arch. Dermat. 74:177-190, August 1956.

the skin In addition the kind of skin cell affected appears of equal importance

Use of staining with toluidine blue for metachromasia, controlled by hyaluronidase acetylation sulfation and chromic acid oxidation disclosed preliminary findings suggestive of a pathologic modification of mucopolysaccharide synthesis by connective tissue cells in lupus erythematosus.

► [It would be interesting to know how far the histochemical characteristics described by Prunieras and Montgomery permit differentiation from photosensitivity dermatoses which clinically often present a knotty differential diagnostic problem.—Eds.]

Serum Anticoagulant Factor in Systemic Lupus Erythematosus. The presence of autoantibodies in lupus erythematosus is frequently demonstrated when hemolytic anemia or thrombocytopenic purpura are manifestations of the disease. The Coombs test and a false positive serologic reaction are indicators of autoimmunologic activity It is therefore of interest to find other immunologic phenomena in lupus erythematosus In recent years circulating anticoagulants have been described and rarely these have been reported in lupus erythematosus The anticoagulant in lupus erythematosus seems to inhibit thromboplastin and is located in the serum gamma globulin Sheldon Swift[1] (Univ of Oregon) observed two patients with lupus erythematosus who had circulating anticoagulants

Woman 47 had been treated since her teens for a recurrent eruption on the trunk and extremities, which was worse in summer and often accompanied by malaise joint swelling and vague aches and pains. At 22, she underwent thyroidectomy At one time she was treated for syphilis because of a positive blood test. Several years later she noted an eruption across the bridge of the nose and on the cheeks. Later L.E. cells were found in the bone marrow and she was treated with cortisone and then prednisone. The maintenance dose of the latter on discharge was 20 mg

She was hospitalized the following year because of an exacerbation of the illness. There were some small superficial ulcerations around the mouth, on the tip of the tongue and on the buccal mucosa. The skin showed minimal increased pigmentation and slight roughening on both cheeks small patches of pigmentation and some erythematous and excoriated areas were seen beneath the breasts, on the abdomen and on the legs. The spleen was palpable. On the second hospital day there were severe depression and malaise, complicated by extensive purpura and oral bleeding Platelet count was 48,000, and the Rumpel Leede test showed

(1) A.M.A Arch. Dermat. 74 296-299 September 1956.

marked capillary fragility Prednisone was increased to 100 mg daily 40 units of corticotropin gel was injected intramuscularly and a whole blood transfusion was given. Response was slow but satisfactory and purpura improved, though gingival bleeding continued for several days. The L.E. test was positive. The direct and indirect Coombs tests and the heterophil agglutination test were negative. The platelet count remained below 40,000, prothrombin concentration was 57% and bleeding and coagulation times were more than 30 minutes. Clot retraction commenced in 3 hours and was completed in 24. A five tube test showed the potency of the circulating anticoagulant. The patient continued to improve and steroids ere gradually reduced. After six months, she appeared in good health and was maintained in complete remission on 25 mg prednisone daily At this time hematologic examination showed complete absence of any antithromboplastin factor

Although some patients with lupus erythematosus have autoantibodies resulting in hemolysis of red cell others show thrombocytopenia, and the excessive liberation of thromboplastin from destroyed platelets could result in production f antibodies against this substance. Therefore it is questionable whether such patients should recei e whole blood transfusions.

Laboratory Studies in Systemic Lupus Erythematosus help establish diagnosis and control treatment, and aid in understanding the disease process according to Stanley L. Lee[2] (Mount Sinai Hosp., New York) Dysproteinemia in lupus is evidenced by hypergammaglobulinemia and abnor mal li er function tests, but these are nonspecific. Four aseral cific manifestations occur False positive serologic te-treatme syphilis may be the earliest sign of the disease an-erpreted as diagnostic f persistent. A positive antig of any one in the skin and (Coombs) from reaction with lipoprotein iharacteristic of der hemolytic anemia. Delayed blood coagatosus nor the vascular promoted by a gamma globulin com-dom were present. conversion of prothrombin to th-ibrosis may be seen in sclerporary complex with thromb- be seen occasionally w th no abnormalities all have a possible similarity to pulmonary istics, occur in one four- further supports the view that col and are not mutually rom common etiologic ba kground. protein anomal pe Gottron) A Bazex and A. Dupré[3] (Tou is present in) eport pertinent case a d consider the disteration t-ation t ongen tal cutaneous atrophies.

——— l., had no history of acrocyanosis or chilblains, but since

(2——

(3 dermat. et syph. 83 644-633, Nov Dec., 953.

some depolymerization and that histone (normally bound tightly to nucleic acid) is no longer identifiable. The L.E. cell phenomenon appears in vivo if susceptible cells are injured and if blood platelets break down. These occur in trauma intercurrent infection and inflammation. Lupus erythematosus which has been considered a skin disease, a vascular disease and a collagen disease may now be considered a disease of protein metabolism

► [Perhaps a "battery" of tests will be gradually developed which may aid in the diagnosis of lupus erythematosus.—Eds.]

Clinical Significance of L.E. Clot Test is reported by Louis A. Brunsting J M Stickney Gertrude L. Pease and William B Reed[3] (Mayo Clinic and Found.) The test performed on 909 patients was positive or doubtfully positive in 14? Of these 112 form or the r ort. About 80% were women 41% l were ar or arthralgia Ka of cutaneous to drugs phadeno

involvement, which dominated the clinical picture throughout the illness.

Woman, 52, had a continuous, brassy nonproductive cough, precipitated by exertion, with moderately severe dyspnea, for three months. No hemoptysis or chest pain was reported. Swelling and aching of the hands were noted, with some blanching of the finger on grasping an object. The cheeks were swollen and blue, and the small joints of the hands were swollen. Muscles of the extremities were painful to pressure and movement. Dysphagia, facial pigmentation and eruption were absent. Results of blood and urine examinations were within normal limits except for increased sedimentation rate of 1 1 mm./minute and increased creatine excretion of 0.37 Gm./24 hours. She seemed to respond satisfactorily t ACTH (25 units twice daily) and cortisone orally (150 mg. da ly) — Despite favorable drop in leukocyte and eosinophil count after hormone therapy deterioration progressed, temperature rose and she died about six weeks after hospitalization.

At autopsy the lungs were unusually resistant on palpa- Microscopically the muscle was arranged in its usual [illegible] showed profound, multifocal exudati and destructive The epidermis was thin and atrophic, with some loss of There ere edema of the collagen, degenerati e [illegible] and homogenization. Some peri ascular inflammation [illegible] lung tissue showed extensive, patchy collapse [illegible] interal eolar chronic inflammatory cell infiltr pointed to tion and edema in some of the expanded [illegible] tures of der

At onset and throughout the illness, [illegible] no typical rash the lungs. Even in the terminal phase [illegible] disease in ts late matomyositis were masked. The [illegible]nophilia were general nor woodlike, edematous character[illegible]really increased creatine stages, although muscle tenderne[illegible] rays were interpreted as Muscle degeneration was re[illegible] not indicati of any one excretion in the urine. Th[illegible] the lesions in the skin and showing chronic interstiti[illegible]cally the lesions in the skin and disease. Although histo[illegible]ic, they were characteristic of der skeletal muscles were [illegible] lupus erythematosus nor the vascular matomyositis. N [illegible] periarteritis nodosa were present. lesions of scleroderm pulmonary fibrosis may be seen n scle-

Marked inf[illegible] t may also be seen occasionally with no roderma [illegible]ation This possible similarity to pulmonary apparent scleroderma further supports the vi w that col chan[illegible]seases ha some common etiologic background. [illegible]rogeria (Type Gottron) A. Bazex and A. Dupré[3] (Tou [illegible]use France) report a pertinent case and consider th dis- ase n r lation to congenital cutaneous atrophies.

Girl, 12, had no history of acrocyanosis or chilblains, but since

(3) Ann. dermat. et syph. 13 [illegible], Nov.-Dec., 951.

birth the hands and feet appeared emaciated. On examination, cutaneous atrophy was evident on the hands and feet, and the skin was as thin as cigaret paper, dry, withered, cold and transparent, to the extent that the underlying tissues, vessels, tendons and bones shone through. There was complete absence of the panniculus adiposus. Atrophy was also present on the palms and soles, insteps, wrists and forearms and even on the thighs, abdomen and thorax, where the skin was traversed by bluish or reddish lines corresponding to veins and arteries. The face had the appearance of that of an old



Fig. 17.—Patient w[illegible] h acrogeria ([illegible] Dupré A[illegible] Ann derm[illegible] et syph. 82:604[illegible] (Courtesy of [illegible] A. and [illegible] 1955.)

person—[illegible] with marked dark circles [illegible] the temples (Fig. 17). The [illegible] unken eyes and scleroderm[illegible] The cutaneous atrophy [illegible] of the bones [illegible] depigmentation [illegible] changes, telangiectatic veins on the rather than [illegible] The hair was fine and dry and the [illegible] and mental development were normal. [illegible] showed onychogryposis. [illegible] the thyroid gland, with a BMR of +26% [illegible] There was mild [illegible] but no clinical [illegible] Development of the breasts and growth of hair [illegible] were normal. An eye examination showed slight [illegible] moderate atrophy of the pigmented epithelium of the [illegible] transparency of the choroid vessels. There were no [illegible]

the skin. In addition the kind of skin cell affected appears of equal importance.

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She was hospitalized the following year because of an exacerbation of the illness. There were some small superficial ulcerations around the mouth, on the tip of the tongue and on the buccal mucosa. The skin showed minimal increased pigmentation and slight roughening on both cheeks, small patches of pigmentation and some erythematous and excoriated areas were seen beneath the breasts, on the abdomen and on the legs. The spleen was palpable. On the second hospital day there were severe depression and malaise, complicated by extensive purpura and oral bleeding. Platelet count was 48,000, and the Rumpel-Leede test showed

(1) A.M.A. Arch. Derm. 74:296-299, September 1956.

recta. Biopsy revealed hyperkeratosis, slightly atrophic stratum granulosum and filamentosum and markedly pigmented basal layer In the epidermis, the elastic fibers were reduced, and in the deeper cutis, they were rather irregular moniliform and transformed into round or extensive orceinophilic masses or into collastin. The collagen fibers were short, thick and without undulation. Small degenerative areas appearing as islands were present in the deep derma. There were no signs of inflammation. The disease neither progressed nor regressed but appeared to be fixed since birth.

Acrogeria (type Gottron) is congenital often involving the female sex Clinically it resembles acrodermatitis chronica atrophicans (Herxheimer Pick) but with no infiltration, erythema, cyanosis, pains, scleroderma or poikiloderma and muscular atrophy Cutaneous atrophy is either localized or generalized, predominantly on the extremities the skin is transparent, withered and wrinkled and shows no folds or crisscross patterns. Appendages of the skin are seldom involved the hair is fine and scarce, but no baldness has been observed. The nails may be normal or fine brittle or onychogryposic Cataracts are absent. The general development is normal, with little endocrine disturbance The disease does not show any evolutionary tendency It is to be distinguished not only from acrodermatitis chronica atrophicans (Herxheimer Pick) but also from a number of congenital cutaneous atrophies. The following summary may clarify the differential diagnosis and also the place of this disease in the category of congenital cutaneous atrophies.

1 Plain atrophy (in early life)
   a) Generalized with general senescence progeria (type Hutchinson-Gilford)—dwarfism and senility since birth, loss of intellect, senile condition of skin, infantile genitalia, complete alopecia, death at 15-25 years geroderma infantilis Variot-Caillian—skin aged and gross too wide, hypoplasia of hair and genitals, longevity normal
   b) Localized on extremities without general senescence acrogeria (type Gottron)
2 Atrophy with poikilodermic changes (in early life)
   a) With cataract and moderate general senescence syndrome of Rothmund
   b) Without either cataract or senescence congenital poikiloderma Thompson
3 Atrophy with poikilodermic changes and cataract (later in life)
   a) With marked sclerodermic changes, but without myotonia syndrome of Werner
   b) With inconstant sclerodermic changes and myotonia myotonic dystrophy Steinert
4 Atrophy with dominant hypotrichosis, dental and ungual dystrophies

birth the hands and feet appeared emaciated. On examination, cutaneous atrophy was evident on the hands and feet, and the skin was as thin as cigaret paper dry withered, cold and transparent, to the extent that the underlying tissues, vessels, tendons and bones shone through. There was complete absence of the panniculus adiposus. Atrophy was also present on the palms and soles, insteps, wrists and forearms and even on the thighs, abdomen and thorax, where the skin was traversed by bluish or reddish lines corresponding to veins and arteries. The face had the appearance of that of an old



Fig 17 —Patient with acrogeria (type ... (Courtesy of Barez, A., and Dupr A.: Ann. dermat. et syph. 82:604-625 1955.)

person—hard and serious, with marked p... dark circles around the sunken eyes and tr... temples (Fig 17) The cutaneous atrophy did... ence of the bones, sclerodermic or poikilodermic changes telangiect... ent veins on the depigmentation. The hair was fine and dry and the ... how erythema, rather thin the big toes showed onychogryposis. Gen... r hyper or and mental development were normal. There was mild hype... nails were the thyroid gland, with a BMR of +26% but no clinical hyp... physical roidism. Development of the breasts and growth of hair in the axilla and pubes were normal An eye examination showed slight vasodilatation and moderate atrophy of the pigmented epithelium of the retina with transparency of the choroid vessels. There were no cata

the Freeman-Sheldon syndrome the causal—possibly identi cal—disturbance sets in earlier than in the syndrome of two sisters, for which the 30th to 35th days may be assumed as the teratogenic term nation period. More defin te evidence of these disturbances was not found, nor could it be stated whether they were hereditary or caused by exogenous en- ironmental damage to the germ The complex of anomalies in the two sisters is a unique variant in the polymorphous group f multiple variations (Pfaundler)

Hereditary Pellagra-Like Skin Rash with Temporary Cerebellar Ataxia Constant Renal Aminoaciduria and Other Bizarre Biochemical Features. D N Baron, C E. Dent H Harris, E. W Hart and J B Jepson (London) describe a new syndrome (H disease) affecting four of eight children of a first cous n marriage The most constant clinical feature was a tendency of the skin to become tough and reddened on exposure to moderate sunlight. In two siblings greater exposure led, more than once, to a severe rash which appeared identical with that of pellagra. Somet mes severe, but fully reversible cerebellar ataxia de eloped with the rash and in one patient fter infecti e disease without rash. The older ffected siblings were mentally retarded

The most specific abnormality identifying the disease is constant gross enal aminoaciduria of unique pattern without other renal dy function. There is also constant large urinary excretion f ndole-3-acetic acid and, less constantly of indican Feces contain moderately increased protoporphyrin. Association of photosensitive skin rash and neurologic abnormal ties suggest porphyria cutanea tarda, but no porphyrin derivatives ar found n the urine and subsequent biochemical studies and closer consideration of the clinical pictu e elim nat this poss bility True pellagra due to diet ary deficiency is not upported by the dietary history or neurologic findings.

Other nstances of H disease may presumabl be seen without skin rash as severe cerebellar ataxia following e- piratory or other infection.

The immediate biochemical d sorder in H disease might be an abnormality of nicot nic cid ut lization. There may be ariation with ge and stress in the requirement for en

[1] Lancet 2 421 28, Sept. 1, 1956

a) With anhidrosis congenital anhidrotic dysplasia
b) Without anhidrosis congenital hidrotic ectodermal dysplasia
5. Atrophy with excess of cutaneous covering and generalized senescence (in early life)

Peculiar Constitutional Anomalies in Two Sisters, aged 12 and 15 are discussed by Georg Klingmuller[4] (Univ of Bonn) The anomalies were remarkably symmetrical and similar and included hypotrichosis and Hertoghe's sign pear-shaped nose in a long oval skull disproportion of the body (narrow upper and broad lower half) silky skin with scanty lanugo hair and numerous striae deviations of 22, 18 and 15 degrees toward the ulnar side of the interphalangeal joints of index middle and ring fingers (in x rays saddle-like epiphysial deformities) shortening of the terminal phalanx of the thumb with koilonychia and of the big toes and flat feet The older sister also had rolled up ear lobes rudimentary papillary ridges and furrows on the fingers, premature epiphysial calcification and atypical calcification of the sella, Schmorl's cartilaginous nodules on the bodies of lower thoracic vertebrae atypical sacral vertebrae and massive acetabular roofs

The great number of anomalies made it possible to classify them as mesenchymal (changes of hand and foot bones, deformities of vertebral bodies and disks atypical calcification of the sella) ectodermal (anomalies of hair and skin pattern) and endocrine The last are represented by numerous striae which according to present concepts are not caused by distention only but by abnormal endocrine function (adrenal cortex) possibly concurring with mechanical trauma. Saddle like epiphysial changes are a nonspecific symptom, seen also in Kaschin Beck disease which occurs in eastern Siberia and is characterized by arthritic pains, articular deformities muscle atrophy struma and scurvy like symptoms. This syndrome is caused by a high iron content in drinking water and has no relations to the syndrome presented by the sisters.

The latter rather has some traits in common with craniocarpotarsal dystrophy (Freeman Sheldon syndrome) distinguished by distant inner corners of the eyes small nose and mouth horny thickening of the skin on the volar aspect of the first phalanges clubfoot and ulnar deviation of hands. In

(4) Hautarzt 7 105-111, March, 1956.

Man, 21 had history of wartlike eruptions since early childhood, ith new eruptions developing from time to time. Three years previously a cavernous hemangioma had been removed from the mediastinum. The palms and backs of the hands showed numerous lesions, 1-7 mm. in diameter elevated bout 1 mm. above the skin surface, with smooth and shining surface and firm consistency. Eruptions on fingers were yellowish and felt hard. Single, large, lenticular papules were seen on the elbows, heels and sternum and smaller ones on the scalp and in the beard and chin region. In the mouth, on mucous membranes of the lips, pale pink, soft papules were present. The external auditory canals had a large number of round pink papules, clotted together each the size of a pinhead. The lesions around the anus resembled condylomata acuminata.

The father and uncle of the patient had had similar though fewer lesions for 50 years, without tendency toward malignant degeneration.

Histologically the lesions on the hands closely resembled warts, with considerable hyperkeratosis and strong stratum granulosum. The papillae were built by all layers of the epidermis. No vacuolation of cells was noticed. The lesions around the anus were granulomas of connective tissue. N inclusion bodies of Lipschütz were detected

Leukoplakia Buccalis and Oral Epithelial Nevi Clinical and Histologic Study was conducted by B E. D Cooke[1] (Guy s Hosp Londo) in 36 patients. In 13 (12 males) the oral lesions were thought to have resulted from smoking Ten were pipe smokers The length of history and severity of symptoms varied considerably from a wh te patch noted on the palat f r 7 years, to loss of taste for 1½ years. In pipe smokers the palate and tongue were ffected n cigaret smokers, the cheeks. The lower lip was involved in three patients, upper n two

Biopsy specimens were taken from cheeks of three patients In all, the surface was well keratinized. In two the epithelium had a well differentiated keratin layer no acanthosis and flat basal layer in one there was melanin in the basal layer pri kle cells and in the corium In one pipe smoker the nfiltrat was dense and associated w th liquefaction degeneration of the basal layer acanthosi d mul tinucleated prickle cells. Investigators are convinced that moking besides aggravating other forms f irritation n the mouth, can also rritate the mucosa itself.

Frictional keratosis was seen in 18 patient in two-thirds the lesion appea ed in the fourth and fifth decades. Soreness wa the presenting symptom when the commissures and

[1] Brit. J Dermat. 66 151 17 May 1954

dogenous nicotinic acid which would explain the clinical deterioration with growth and infective disease and the possible improvement in adult life In such a primary defect of indole metabolism the other biochemical abnormalities *would have to be considered* as cellular metabolic consequences of apparent nicotinamide deficiency However the opposite situation is equally plausible—a primary disorder of amino acid transport leading to development of an abnormal gut flora which distorts normal nicotinic acid utilization.

Congenital Telangiectatic Cutis Marmorata. Luis E. Pierini and David Grinspan[8] (Buenos Aires) report two cases in men aged 48 and 28, whose condition had remained unchanged since birth No other members of the families were similarly afflicted The lesions resemble those of cutis marmorata but the network is scarlet red and not cyanotic. Other lesions combine in the form of diffuse flat vascular blemishes of bluish color similar to flat angiomas or telangiectasias of vivid red. The first patient had thick varicose cords and the deep venous network was visible through the thin skin The lesions were localized in the classic sites, i e on all parts of the body except the nose lips, ears genitalia, palms soles and midline The second patient had, in addition lesions in the buccal nasal and pharyngeal mucosa that caused epistaxis and bleeding of the mouth. The palms, soles and scalp also were affected. Both patients had torpid ulcers on the heels apparently of post traumatic origin which in the second patient resulted in considerable loss of tissue, with vegetations and articular retraction Neither patient showed any clinical abnormality

Histologic examination showed passive congestion through ectasia which appeared to originate in the vessels of the subcutaneous and hypodermic plexuses and extended to subpapillary venules and capillaries of the papillary layer where anoxia caused edema and perivascular lymphocytic *infiltration Generally there was no formation of new blood* vessels In the hypodermis were large varicose veins. An ulcer in the second patient was histologically similar to common varicose ulcers.

Verrucosis Generalisata. E. H Hermans Sr and J P Vater[9] (Rotterdam) report *cases in three members of a family*

(8) Arch argent. dermat. 5:295-310, December 1955
(9) Acta dermat venereol. 36 112-120, 1956.

Man, 21 had history of wartlike eruptions since early childhood, ith new eruptions developing from time to time. Three years previously cavernous hemangioma had been removed from the mediastinum. The palms and backs of the hands showed numerous lesions, 1-7 mm. in diameter elevated about 1 mm. above the skin surface, with a smooth and shining surface and firm consistency Eruptions on fingers were yellowish and felt hard. Single, large, lenticular papules were seen on the elbows, heels and sternum and smaller ones on the scalp and in the beard and chin region. In the mouth, on mucous membranes of the lips, pale pink, soft papules were present. The external auditory canals had large number of round pink papules, clotted together each the size of a pinhead. The lesions around the anus esembled condylomata acuminata.

The father and uncle of the patient had had similar though fewer lesions for 50 years, without tendency toward malignant degeneration.

Histologically the lesions on the hands closely resembled warts, ith considerable hyperkeratosis and a strong stratum granulosum. The papillae were built by all layers of the epidermis. No vacuolation of cells was noticed. The lesions around the anus were granulomas of connective tissue. No inclusion bodies of Lipschütz were detected.

Leukoplakia Buccalis and Oral Epithelial Nevi Clinical and Histologic Study was conducted by B E. D Cooke[1] (Guy s Hosp London) in 36 patients. In 13 (12 males) the oral lesions were thought to have resulted from smoking Ten were pipe mokers. Th length of history and severity f symptoms varied cons derably from a wh te patch noted on the palate for 7 years, to loss of taste for 1½ years In pipe smokers the palate d tongue were affected n cigaret smokers, the cheeks. The lower lip was invol ed in three patients, upper in two

Biopsy specimens were taken from cheeks of three pa tients. I all the surface was well keratinized. In two the epithelium had a well differentiated keratin layer no acan thosis and flat basal layer in one there was melanin in the basal layer prickle cells and in the corium. In one pipe smoker th i filtrat was dense and associated with liquefaction degeneration of the basal layer acanthosi nd mul tin cleated prickl cells. Investigators are convinced that smoking besides aggravating other f rms of irritation in the mouth, can also irritate the mucosa tself.

Frictional keratosis was seen in 18 patients in two-thirds the lesion ppeared in the fourth and fifth decades Soreness wa the presenting ymptom when the commissures and

(1) Brit J Dermat 66 151 174, May 1954

tongue were involved but lesions on the occlusal line of the cheeks were often incidental findings. Most commonly the occlusal line was involved Histologically the first reaction of the nonkeratinized buccal mucosa to friction was slight *acanthosis* and parakeratosis. Then followed an inflammatory reaction in the corium with dilated capillaries and lymphocytic and plasma cell infiltration. Histiocytes laden with hemosiderin often gave evidence of old extravasation of blood The most severe reaction was noted in the commissures with broadening and deepening of the epithelial ridges



Fig 18.—Oral epithelial nevus (Courtesy of Cooke B E D. Brit J Dermat 68 151 174 May 1956)

overlying a diffuse dense chronic inflammatory reaction in the corium

Leukoplakia was due to syphilis in three patients Histologic examination showed the epithelium keratinized in a regular manner with a well marked keratin layer granular layer and only slight acanthosis Many dilated capillaries were found in the corium around many of these was a mild infiltrate of lymphocytes and plasma cells

Idiopathic keratosis was seen in two patients Most lesions were diffuse and symmetrical *on either the tongue or cheeks,* which suggests systemic factors rather than local causes Histologic examination in one case revealed a well marked keratin and granular layer and slight acanthosis overlying a normal corium.

An oral epithelial nevus was observed in six patients. Being symptomless it may remain unnoticed by the patient The affected area is dense white, well defined and raised above the level of the surrounding mucosa. The mucosa is normal in appearance. The white patch has a regular wrinkled appearance without tessellation or wartiness on the floor of the mouth and on the gum. On the floor of the mouth and ventral surface of the tongue it resembles the undulations left in the sand by an ebbing tide (Fig 18)

The most important condition to consider in differential diagnosis of leukoplakia is lichen planus. In contrast to leukoplakia, it is more common in women. There will be a history of the lesions appearing and disappearing The commissures are usually spared, and the papules are usually in a characteristic symmetrical pattern

► [An informative article which calls attention to epithelial nevi occurring on the oral mucosa which at times clinically resemble thickened plaques of leukoplakia (or leukokeratosis) or lichen planus We have seen lesions almost identical with the one in Figure 18 diagnosed clinically as precancerous leukoplakia. According to Cooke, the histopathology cause and prognosis of this nevus is different from leukoplakia Biopsy still remains the only dependable method for differentiating these whitish plaques which occur on the oral mucosa.

We have had a patient under observation for a number of years with an oral nevus which involves the buccal mucosa as well as the mucosal parts of the lips. The clinical findings which have not changed over the years consist of a very fine reticular whitish lacework on a somewhat bluish translucent mucosa. Histologically there is a moderately and irregularly acanthotic epidermis with some thickening of the horny layer Very little cellular reaction is seen in the underlying corium. The superficial vessels are dilated.—Eds]

Ocular Pemphigus with Generalized Bullous Eruption. R E Church and I B Sneddon[2] (Sheffield, England) present a case as further evidence that ocular pemphigus is distinct from pemphigus vulgaris.

Woman, 70 had a history of soreness of mouth and vulvar irritation at age 64, followed by blisters in the pubic and perineal areas which left extensive erosions after rupture. There were intermittent minor exacerbations, but later a severe relapse, with blisters in the mouth and on the trunk, axillae, groins, vulva and around the anus. There had been bullae and erosions on the eyelids which progressed to marked adhesions in the right and conjunctival shrinkage in both eyes A histologic section showed a subepidermal bulla in the upper dermis with no acantholysis. The bulla had rounded margins and contained many eosinophils and a few neutrophils. Treatment consisted of ACTH, up to 50 mg./day, and then δ-cortisone, up to 80 mg /day with a maintenance dose of 40 mg /day After three weeks,

(2) Brit J Dermat 68 128 131, April, 1956.

tongue were involved but lesions on the occlusal line of the cheeks were often incidental findings. Most commonly the *occlusal line* was involved Histologically the first reaction of the nonkeratinized buccal mucosa to friction was slight *acanthosis* and parakeratosis Then followed an inflammatory reaction in the corium with dilated capillaries and *lymphocytic* and plasma cell infiltration Histiocytes laden with hemosiderin often gave evidence of old extravasation *of blood* The most severe reaction was noted in the commissures with broadening and deepening of the epithelial ridges



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loon g degeneration) many eosinophils and monocytes, but the composition varied occasionally cellular elements were missing Ballooning degeneration of epithelial cells occurs mainly in pemphigus ulgaris (pemphigus cell) but was also seen in bullous viral diseases, Darier's disease, Hailey's disease, psoriasis pustulosa and even in banal pustules. In smears from pustules from 7 of 50 patients with various dermatoses, cells were found that corresponded completely to pemphigus cells. Moreover smears from cantharidin blisters in normal persons also showed numerous epithelial cells with ballooning degeneration.

It is concluded that so-called pemphigus senilis may not be an entity Some cases are better included in dermatitis herpetiformis, others in pemphigus vulgaris Furthermore, smears from the bulla floor and histology may not be sufficient to separate pemphigus senilis from pemphigus vulgaris.

► [Findings such as these favor the opinion of those who are inclined to lump together under the diagnosis of pemphigus those bullous eruptions of the skin hich have features somewhat atypical for basic pemphigus vulgaris. Just as certain other dermatoses, g psoriasis, may not have all the usual and typical characteristics when affecting senile skin, such may ell be the case with pemphigus. The results of these studies also point out that cytodiagnostic study of cells from the floor of the bulla alone is by no means certain diagnostic test for pemphigus. Nevertheless it must be stated that in *the hands of experts* the procedure suggested by Tzanck can be highly valuable in the differential diagnosis of bullous diseases.

In view of their relatively benign course and tendency to remission, it is obvious that the inclusion of cases of pemphigus senilis, pemphigoid, etc in therapeutic studies with ACTH and corticosteroids of the cortisone type, may well lead to erroneous conclusions as to the efficacy of the medicaments.—Eds.]

Pemphigus and Duhring Brocq Dermatitis Cytopathologic Study of 176 cases of pemphigus foliaceus, 12 of pemphigus ulgaris, 7 of pemphigus vegetans 6 of pemphigus frusto [the author here is apparently referring to pemphigus erythematosus (Senear Usher pemphigus)—Eds.] 13 of Duhring Brocq dermat tis 3 of erythema multiforme and 4 f bullous epidermolysis is reported by Benjamin Zilberberg Artificial bullae were produced experimentally n patients with pemphigus and other dermatoses and in normal subject

From this study Zilberberg concludes that acantholysis co titutes the basis of various types of pemphigus. Pem

( ) Arq dermat. e sif Sao Paulo 41:123, 195

the active lesions healed and though the adhesions were unaltered, the eyes were more comfortable than they had been for several years. Weight and blood pressure were constant during therapy

The lesions were more extensive than usual in ocular pemphigus and the recurrent bullae appeared on a circumscribed area leading to scarring The subepidermal bulla with no acantholysis was significantly different from findings in pemphigus vulgaris thus supporting the view that these are separate entities. The patient responded favorably to steroid treatment but it was not possible to control all mucosal lesions

Differential Diagnosis of Pemphigus Vulgaris by Smears from Floor of Bullae is discussed by Gerd Klaus Steigleder[3] (Univ of Frankfurt) Histology and scrapings from the floor of bullous lesions, although of high diagnostic value in pemphigus vulgaris and dermatitis herpetiformis are less valuable in cases that formerly were considered either pemphigus or dermatitis herpetiformis and were called pemphigus senilis (bullous) pemphigoid or parapemphigus. Observation of 20 cases of senile pemphigus (14 in women) revealed the average age of patients to be over 70

Bullae showed less tendency to spread, persisted longer and the eruption was less extensive varying in the distribution of bullae, in senile pemphigus Involvement of mucous membranes was rare nail dystrophy was in contradistinction to pemphigus vulgaris never seen Erythematous and urticarial lesions alternated or were concurrent with bullous eruptions. The course also varied, some patients remaining free from disease after a single attack others only after ACTH and cortisone were used. Disturbed liver function was often observed (e.g positive Takata reaction) Autopsies revealed fatty degeneration of the liver with no intercurrent disease as in pemphigus vulgaris Changes in serum protein levels were not uniform but decreased levels of total serum proteins with markedly reduced levels of serum albumin were often observed Histology revealed the presence of subepidermal bullae. However in pemphigus vulgaris, large bullae also may become subepidermal

In senile pemphigu smears from the bulla floor showed numerous epithelial elements (even epithelial cells with bal

(3) Arch. klin. u. exper Dermat. 202 1 9 1955.

looning degeneration) many eosinophils and monocytes, but the composition varied occasionally cellular elements were missing Ballooning degeneration of epithelial cells occurs mainly in pemphigus vulgaris (pemphigus cells) but was also seen in bullous viral diseases, Darier's disease Hailey's disease, psoriasis pustulosa and even in banal pustules. In smears from pustules from 7 of 50 patients with various dermatoses, cells were found that corresponded completely to pemphigus cells Moreover smears from cantharidin blisters in normal persons also showed numerous epithelial cells with ballooning degeneration.

It is concluded that so-called pemphigus senilis may not be an entity Some cases are better included in dermatitis herpetiformis, others in pemphigus vulgaris. Furthermore smears from the bulla floor and histology may not be sufficient to separate pemphigus senilis from pemphigus vulgaris

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In view of their relatively benign course and tendency to remission, it is obvious that the inclusion of cases of pemphigus senilis, pemphigoid, etc., in therapeutic studies with ACTH and corticosteroids of the cortisone type, may well lead to erroneous conclusions as to the efficacy of the medicaments —Eds]

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From this study Zilberberg concludes that acantholysis constitutes the basis of various types of pemphigus. Pem-

( ) Arq dermat. e sif São Paulo 43-123, 955

phigus does not exist without acantholysis although the latter may exist without pemphigus. Acantholysis is the characteristic feature, not the site of the vesicle Cytohistologic examination is preferred for diagnosis of these two conditions and is the best method of identifying the type of pemphigus and differentiating it from pemphigoid lesions.

In cases diagnosed clinically as chronic pemphigus vulgaris there are two histologically different lesions One is characterized by acantholysis forming intraepidermal bullae the other by some subepidermal bullae with distending edema without acantholysis (Duhring Brocq dermatitis) There are two types of Duhring Brocq dermatitis with identical histologic structure one extremely benign often herpetiform and the other essentially monomorphous often malignant with clinical characteristics similar to those of pemphigus vulgaris

In the study of these diseases serial sections are indispensable particularly in Duhring Brocq dermatitis because of the possibility of anomalous localizations i.e. partially subepidermal and totally intraepidermal leading to confusion with pemphigus The presence of a false Nikolsky sign or of subepidermal displacement by trauma during biopsy indicates an abnormality often mortal in Duhring Brocq disease which in these cases is always monomorphic. Classic herpetiform types rarely present cellular displacement and their course never or rarely is malignant Consequently this sign has great prognostic value

Cytologic changes in pemphigus by their similarity to those of vesicular viral diseases suggest that this may be due to a virus

The Nikolsky sign when studied histologically or cytologically has considerable value in diagnosis of various types of pemphigus and pemphigoid lesions It is suprabasal in pemphigus vulgaris and pemphigus vegetans subcorneal or subgranular in pemphigus foliaceus and pemphigus frusto and subepidermal in pemphigoid conditions. In the last instance the Nikolsky sign is a false rather than a true one which is found exclusively in pemphigus

Bullous Dermatoses in the Southern Negro. N Medd Henington C. Barrett Kennedy and Kenneth B Snider[5] re-

(5) South. M J 49:39-46, January 1956.

port on 105 cases in Negroes seen at Charity Hospital, New Orleans, during five years. In this period there were 1,700 admissions to the dermatologic clinic, of whom 779 (48%) were Negroes. Although protected by their pigment, Negroes ar susceptible to photosensitization but seldom exfoliate. Negroes have an oily seborrheic skin and show almost complete lack f resistance to pustular dermatitis. Bullous dermatoses are more frequent in the Negro than in the white and more serious as shown by 7 fatal cases among the 105. In the Negro associated erythema may not be evident early and in general bullous lesions are violent widespread, numerous and large and involve the mucous membra es.

Inf eq ent varieties of bullous dermatoses seen were two cases of va cinia n children two of pemphigus erythematosus (Senear Usher) in which lesions of pemphigus were distributed as n lupus erythematosus four of dermatitis herpetiformis two occurring during pregnancy and all responding to sulfapyridin six of erythema multiforme n all of which the patients were acut ly ill in contrast to the usual course in white patients and two of lupus erythematosus which responded well to steroids.

The largest groups of bullous dermatoses included 13 cases f pemphigus, 21 of herpes zoster 22 of impetigo and 33 of drug eruptions. There were four deaths in the pemphigus group. The man festations of this disease are bizarre. Eight patients in luding three who died, were treated with steroids although i general treatment was difficult. One death, from lymphosarcoma, occurred in the herpes zoster group. Man festatio s and results of treatment were simila to those white patients with unusually good response to aureomycin. Impet go is seen primarily n infancy and youth t has pecial predilection for the head, neck and scalp which increases da ger of the disease. The most serious complication in the 22 cases was acute glomerulonephriti present n 5. In the drug erupt ons group 17 pat ents had used patent medicine 666. Negroes are unusually susceptible to dr g nd thei reactions are severe and sometimes fatal. Drugs l ed, n th order of their frequency were penicillin sulfonam des barbiturates, salicylates phenolphthalein and dilantin. Reactions to "666, which may contain quin ne o antipyrine may be of varying duration, with bullae on the

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Two cases were typical of pustular bacterid described by Andrews, with more acute lesions eczematoid histopathology and cure on removal of a septic focus in the tonsils in one.

► [There are many transitional forms between the categories of pustular eruptions described here by Pierini and variety of eczematous eruptions of the hands and feet which may have pustular components.

No matter which particular member of this group of eruptions one is confronted with, therapy often is difficult. What is successful in the management of one case is inadequate in another apparently similar case. Tonsillectomy in one case, extraction of teeth in another x-radiation in a third, oral antibiotics or corticosteroids in still another (see editorial comment to following abstract) may prove beneficial. For the time being the best approach is to select the most suitable form of therapy on trial and error basis for each patient, using a carefully taken history physical examination and past experience as guide. The real hope for improved therapy lies in discovery of the causal mechanisms producing the pustular eruptions which eventually will permit etiologic classification. —Eds.]

Pustular Psoriasis. Giambattista Marson (Univ of Padua) eports a case. The pustules constitute a particular ariety of psoriasis rather than a complication of it. The condition can be localized to an extremity or diffuse, and is characterized by periods of quiescence alternati g w th periods f subacute or acute exacerbation. It is little influenced by the standard drugs that are partially effective in psoriasis but is ignificantly improved by cortisone.

Man, 58, had erythematous squamous patches of psoriatic nature and other red patches, with but little exudate or with scaly crusts that could be easily removed, on parts of the body typical for psoriasis. The lesions slowly became more hyperkeratotic, and isolated pustules or groups of pustules appeared on the healthy skin and in the patches. Early histologic studies of sections of affected skin showed parakeratosis and papillomatosis, with polynuclear and mononuclear lements Over four year period the clinical symptoms and histologic findings suggested pustular psoriasis. Topical treatment and prolonged and massive penicillin therapy during three hospital admissions failed to bring about improvement, and the exudate increased. Cortisone in daily doses of 150 mg for three 15-20 day cycles, with treatment-free interval of week between each cycle, produced a gradual attenuation of the pustules first and of the erythematous squamous patches later.

The effect of cortisone on pustular psoriasis is only tran-

) Minerva dermat. 26:398-40 December 951.

face genitalia, hands and feet and in the mouth. Treatment consists of drug withdrawal supportive measures and steroids

It is concluded that skin diseases in Negroes and whites differ in certain respects complicating diagnosis and therapy but racial differentiation must not be carried too far

► [While the differences in the bullous diseases between white and Negro patients appear not to be of major importance, their drug habits differ substantially The editors also have seen a number of cases of drug eruption due to "666 in Negroes but cannot recall a single white patient who gave a history of having taken this particular remedy!—Eds.]

Acrodermatosis Pustulosa. Dagoberto O Pierini[6] (Buenos Aires) describes six cases exemplifying the three main types of this condition Two cases were instances of acrodermatitis pustulosa perstans localized and generalized respectively In the first trauma clearly precipitated the lesion localized in the hands with purulent phlyctenae extending eccentrically in the palms and flat pustules in the periungual region. Some nails were lacking and those remaining presented profound changes Hemolytic streptococcus was found in the phlyctenae. Principal histologic findings were minimal parakeratosis acanthosis with papillomatosis spongoid degeneration and intense exocytosis of polynuclear neutrophils which also filled the blisters on the thickened mucosa. In the second case without previous trauma, the disease was episodic. Lesions first localized on the extremities, then became generalized over almost all the skin with erythematopustular herpetiform plaques followed by much desquamation (erythroderma exfoliativa) At this stage the general state changed and improved with regression of skin lesions to their original sites (hands feet and skin folds) In both cases, all treatment failed.

The third and fourth cases represented the second group palmoplantar psoriasis pustulosa. In the former the lesions originally resembled acrodermatitis continua i.e., with swelling and periungual pustules Later typical symptoms of common psoriasis developed in other parts of the skin which persisted after periungual lesions were cured by x ray therapy Aside from somewhat larger microabscesses the histologic picture resembled psoriasis Conversely in the fourth case the psoriatic nature could be confirmed by clin

(6) Arch. argent. dermat. 5 217 256, September 1955.

cal appearance of the lesions in some stages and especially by a histopathologic picture identical to psoriasis. In this case all therapy failed, including x-ray treatment and extirpation of septic foci.

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(7) Minerva dermat. 30 300 44 December 1955

sitory and symptomatic and is ascribed to the inhibiting power of the drug on cell permeability and on the migration process of the stable and mobile elements of the connective tissue and of the blood.

► [It is our experience also that cortisone administered systemically is beneficial in palmar and plantar dermatoses which fit the picture of pustular psoriasis. A dose of 150 mg daily is usually sufficient. When discontinuing the drug, however we prefer to taper off the dose gradually rather than to stop it abruptly In this way one stands a better chance of finding the maintenance dose and less chance of causing symptoms as a result of leaving the adrenal cortex at rest and unprepared to take on its normal responsibilities. In view of the usual chronic and recurrent course of this dermatosis, cortisone therapy is likely to be necessary over a prolonged period.

In some cases of chronic and recurrent pustular eruptions on the hands and feet, wide spectrum antibiotics and sulfonamides have been effective. —Eds.]

Erythrodermic Psoriasis in Children. Psoriatic exfoliative erythroderma is extremely rare in children. Frances Pascher and William S Wood[8] (New York Univ Post-Grad. Med. School and Skin and Cancer Unit) report two cases.

Boy 13 noticed cutaneous symptoms one month after recovery from infectious hepatitis. Cracks between the toes and fingers were gradually followed by a dry somewhat pruritic, diffuse erythematous eruption resistant to conventional treatment.

The scalp was covered with micaceous scales and the glabrous skin was the seat of a diffuse moderately bright erythroderma with silvery white scales. The palms and soles were hyperkeratotic and fissured. Finger nails were lusterless and pitted and showed longitudinal ridges. General physical examination revealed no other abnormalities. Liver function tests were normal. Histopathologic examination revealed a fairly regularly acanthotic epidermis with elongated and club-shaped rete pegs. The suprapapillary plates were thinned, and there was considerable parakeratosis. A Monro abscess was seen in one area. Superficial capillaries were dilated and there was a diffuse, mild nonspecific cellular infiltration in the subepidermal corium. Edema of the papillary bodies was also observed.

Except for bland creams which eased the dryness, the topical approach was futile. However response to daily injections of 40 units of corticotropin gel was dramatic. Improvement was striking in three days and in less than a week the skin appeared normal, except for the scalp, nails, palms and soles, which showed no commensurate improvement. A change to hydrocortisone acetate, 80 mg daily in divided doses, was made at the end of the first week. Response to this hormone was equally satisfactory The maintenance dose was 10 mg four times a day An attempt to reduce the dose further was followed promptly by an exacerbation, the first sign of which was pinpoint-sized erythematous follicular lesions (psoriasis follicularis) on the trunk and extremities.

(8) A.M.A. Arch. Dermat. 74:173-176, August, 1956.

Except for a superficial pyoderma, which responded to an antibiotic cream, no complications were encountered. Discontinuation of corticosteroid therapy was followed by total relapse in three weeks.

The response to diluted potassium arsenite (Fowler's) solution (1:3) in ascending doses was almost as prompt as to corticosteroids. Clearing was noted after 0.6 ml. three times a day and improvement was striking when a dose of 0.9 ml. three times daily was reached. The remission thus induced lasted three weeks. A second course of arsenotherapy was discontinued because of intolerance.

Prednisone 20 mg. daily improved the condition as dramatically as the former steroids. At the end of the first week it was possible to reduce the dose by 5 mg./day; later 5 mg. twice daily sufficed to maintain suppression. The patient has been well enough to attend school.

In the other patient, a girl aged 7, the maintenance morbistatic dose proved to be high, 40 units of corticotropin gel weekly and 40 mg. hydrocortisone acetate daily. Prolonged administration of these hormones in so young a patient, particularly in view of an episode of glycosuria, appeared inadvisable and was discontinued.

► [Psoriatic erythroderma appears to respond as well to corticosteroids in children as in adults. The corticosteroids and ACTH are ordinarily not considered of value in the management of nonerythrodermic psoriasis. Our own experience has shown that if large enough doses are administered even the most severe cases of psoriasis will respond as long as the large doses are maintained. The size of the dose required for psoriasis in adults is usually prohibitive and other forms of therapy should be used. —Eds.]

Experience with Köbner's Reaction. Leonardo Nardelli[7] (Rome) found that Köbner's reaction is positive in all patients with psoriasis, although at times it is extremely irregular, confined to particular areas of skin and of short duration. The intensity of the reaction varies according to the phase, development and severity of the psoriasis. When the disease is mild, circumscribed and stationary, the reaction is often negative for large areas of skin. This appears to indicate that vast areas lack or have a diminished psoriatic predisposition or irritation and that this varies from person to person, and in the same person at different times and in different zones of skin. The reaction diminishes or even becomes negative in the long quiescent periods of the disease and during remissions (summer). It becomes positive again in 50-70% of cases in the winter. It is almost always negative in areas in which a psoriasis lesion was cured or inflammation was caused by treatment (zone of inhibition).

(7) Minerva dermat. [illegible], June, [illegible]

When this zone of inhibition or refractoriness to Köbner's reaction extends beyond the healed area and to the entire skin it suggests that the psoriasis is undergoing a long remission. Köbner's reaction can be inhibited locally by intradermal or subcutaneous injection of substances (cortisone, epinephrine, lysates of epidermis) that cause a local inflammatory reaction. Only if the inhibition is independent of inflammatory episodes and is of long duration can it be ascribed to a specific action of the injected substance.

► [It is a common experience that the Köbner phenomenon is much more likely to occur in acute and spreading psoriasis than in the chronic torpid form and it comes as somewhat of a surprise that the injection of certain substances which produce inflammation inhibits rather than causes a Köbner phenomenon.

Kuznitzky (*J. Invest. Dermat.* 14:435, 1950) discussed a phenomenon perhaps closely related to the inhibition referred to by Nardelli, which he called "the intermediate zone (immune, refractory, anemic, depigmented zone)." —Eds.]

Granulomas of Axillae Caused by Deodorants were observed by Louis Rubin, Albert H. Slepyan, Leonard F. Weber and Irene Neuhauser[1] (Univ. of Illinois) in four patients. Although clinical appearance and results of pathologic examinations were consistent in all patients, the exact cause of the granulomatous lesion remained unknown. The changes were well illustrated by the following patient.



Fig. 19.—Dull, brownish red pinhead- to matchhead-sized papules in axilla. (Courtesy of Rubin, L., et al.: J.A.M.A. 162:953-955, Nov. 3, 1956.)

(1) J.A.M.A. 162:953-955, Nov. 3, 1956.

Woman, 56, applied a stick deodorant to the axillae, which were shaved next morning. Two days later a moderately pruritic eruption appeared. On examination, five weeks later, there were innumerable dull, brownish red, pinhead- to matchhead-sized papules in both axillae (Fig. 19). Many were shiny and somewhat translucent. Pricking the lesions revealed no fluid. On diascopic pressure, apple jelly color was noted. After five weekly treatments with superficial x-rays and application of hydrocortisone in lotion and cream form, there was little change except for a somewhat more yellow color and slight scaling. Sections of the specimen stained with hematoxylin and

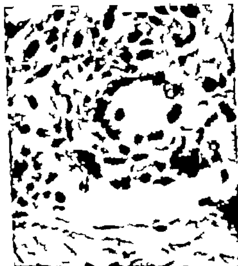


Fig. 20.—Section from biopsy specimen of papule. (Courtesy of Rubin, L., et al.: J.A.M.A. 162:953, Nov. 3, 1956.)

eosin showed the essential pathologic changes in the upper corium. A fairly dense granulomatous mass consisting of epithelioid cells, Langhans giant cells, lymphocytes and an occasional eosinophil surrounded a hair follicle (Fig. 20). Many small blood vessels were included in the granulomatous area. Polaroscopic examination did not reveal foreign material.

This chronic condition, though evidently resistant to treatment, may be alleviated in the acute stage by topically administered steroids.

► [There is little doubt that deodorants played an important role in the cases described by Rubin *et al.* as well as in those seen by the editors and other dermatologists. Moreover, it seems clear that in many of these eruptions a particular brand of "stick" deodorant was involved. However, there were also some cases in which a liquid or cream deodorant had

been used (which did not contain sodium zirconium lactate, the principal suspect thus far in the stick deodorant). Thus the etiology and pathogenesis of these persistent and highly annoying eruptions still are unclear. —Eds.]

Fox Fordyce Disease in the Male. Review of Literature and Report of Case. Fox Fordyce disease in males is infre-



Fig. 21. Lesions in right and left axillae. (Courtesy of Winkelmann, R. K., et al.: A.M.A. Arch. Dermat. 74:479-483, November, 1956.)

quent but not rare. Richard K. Winkelmann, Robert R. Kierland and Hamilton Montgomery[2] (Mayo Clinic and Found.) report *the following case, the 24th in the literature.*

Man, 49, had a pruritic papular eruption beginning one year before, after use of deodorants. *It commenced in the left axilla and* shortly after in the right, as *flesh-colored pruritic papules.* Discontinuing the deodorant did not end the *pruritus and new lesions* developed. One month after onset, a similar eruption appeared about

(2) A.M.A. Arch. Dermat. 74:479-483, November, 1956.

the areolae and in the suprapubic area. The patient noted pruritus was worse under stress, but could not relate the process to any other factor. During the year the eruption was present, the only change had been a tendency for lesions to turn deep brown. Two x-ray treatments were without result. Local medication, including hydrocortisone, had given no relief. One month before hospitalization, a tender nodule developed in the left axilla. Physical examination revealed symmetrical papular eruption of the axillae, areolae and suprapubic region. Papules ranged in color from flesh to brown and were separated by areas of normal skin. On the areolae they were arranged in concentric circles and were largely peripheral. Only in the axillae was there loss of hair. The axillary eruption is shown in Figure 21.

Histologic examination revealed hyperkeratosis and acanthosis. Mucin was abnormally abundant in sections of biopsy specimens from all three regions. It was found free in the cutis and in degenerate apocrine glands. Although resistant to diastase, this mucin showed positive reaction to periodic acid-Schiff reagent. It was slightly basophilic and negative to sudan black B. In sections of axilla and areola, successive steps of apocrine gland degeneration were evident. Coils of normal gland were found next to those with completely trophic epithelium.

Fox Fordyce disease in the male is identical with that in females in appearance and location of the lesions, clinical course and lack of response to therapy. The mucinous change found in these biopsy specimens may explain the chronic clinical course of this condition.

Apocrine Sweat Retention in Man. II. Fox Fordyce Disease (Apocrine Miliaria). Walter B. Shelley and Edwin J. Levy[3] (Univ. of Pennsylvania) present 15 cases and histologic evidence to support their thesis that Fox Fordyce disease is an apocrine gland type of miliaria.

Clinically the disease is a chronic pruritic papular eruption, usually occurring in women and localized to the apocrine gland areas, axillae, pubes, labia, perineum, areolae of breast, presternal areas, umbilicus and medial surface of the upper thigh. It has not been seen before puberty and is rare after the menopause. The papules are discrete, firm, flesh colored and perifollicular. They present a smooth, rounded dome-shaped appearance with a central punctum which can be expressed. After exercise or emotional tension the papules show a minor increase in size, and, on stretching the skin, a linear arrangement. There are decreased sweating

[3] A.M.A. Arch. Dermat. 73:38-49, January, 1956.

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Fig 21—Lesions in right and left axillae. (Courtesy of Winkelmann, R. K et al. A.M.A. Arch. Derm 74 479-483, November 1956.)

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(2) A.M.A. Arch. Dermat. 74 479 483, November 1956.

ported with irradiation. Included in the differential diagnosis are acanthosis nigricans, leiomyoma, lichen nitidus, lichen planus, localized neurodermatitis, nevus, sebaceous adenoma, syringoma, syringocystadenoma and verruca plana. Various theories have been advanced as to the cause of this disease, among them plugging of the apocrine sweat duct, with extravasation of the trapped sweat out of the duct into the epidermis.

In their study of 14 females and 1 male with Fox Fordyce disease the authors demonstrated complete apocrine anhidrosis. Although eccrine sweating may be normal, apocrine sweat never appears on the skin in response to specific stimuli. This anhidrosis does not result from impairment of the secretory portion of the gland, but from keratotic plugs in the apocrine duct orifices. The duct ruptures under the pressure of apocrine sweat secretion producing the intraepidermal sweat retention vesicle, which is pathognomonic of the disease (Fig 22). The clinical picture can readily be correlated with the histopathology and the disturbed physiology of apocrine gland secretion—i.e., age and sites of occurrence primary lesion (the papule) and major symptom (paroxysmal pruritus) which occurs only when the paraductal sweat retention vesicle ruptures intraepidermally. The failure of therapy is direct result of inability to inhibit apocrine secretion. The endocrinologic approach gives the greatest promise.

This study clearly places Fox Fordyce disease into the group of sweat retention dermatoses generically called miliaria. Apocrine miliaria is suggested as a synonym. The disease is analogous to miliaria rubra, in both of which epidermal extravasation occurs about the terminal sweat duct.

► [Fox Fordyce disease-like eruptions due to antiperspirants also must be included in the differential diagnosis. This as yet not completely clarified syndrome, recently noted in the United States especially after the use of certain "stick" deodorants, presents distinct therapeutic challenge and possible medicolegal problems. As stated in the original article, the therapy of Fox-Fordyce disease is generally unsatisfactory. Unfortunately the syndrome produced by certain deodorants also has shown remarkable resistance to treatment.—Ed.]

Simultaneous Dyshidrosis in Monozygotic Twins during Separation was observed by Allan L. Lorincz and Franklin H. Kramer[1] (Walter Reed Army Med. Center)

Male twins, 21, were judged monozygotic on the basis of identical

1 A.M.A. Arch. Dermat. 2[illegible]: 212, September 1956.

(eccrine) and interference with hair growth in the affected areas The major symptom is localized, severe, paroxysmal pruritus initiated by emotional crises sexual activity excitement or even exercise. It is worse at night and before

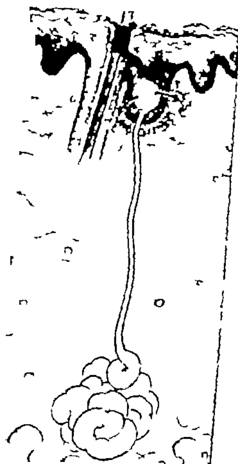


Fig 22.—Significant events in Fox Fordyce disease Closure of terminal apocrine sweat duct by keratin is followed by dilatation of apocrine sweat gland unit, ductal rupture and formation of sweat retention cyst in epidermis. Epidermal damage is followed by acanthosis and inflammatory response in dermis (Courtesy of Shelley W B and Levy E. J A.M.A. Arch. Dermat. 73 38-49 January 1956.)

menstruation Histologic findings are hyperkeratosis with plugging of the apocrine sweat gland duct and associated hair follicle acanthosis and spongiosis chronic inflammatory changes in the dermis and dilatation of the apocrine sweat gland acini Therapy short of surgical excision is generally unsatisfactory although some good results are re

it developed without such exposure and that during periods of little emotional stress A could well tolerate severe exposure to harsh contact hand irritants.

► [Another striking example of congenital factors influencing disease. Histologic and histochemical studies of tissue from the affected parts in both twins perhaps would be helpful in revealing the anatomic physiologic or biochemical background for the aberrant responses of their skin to various stimuli —Eds.]

Hyperhidrosis of Hands in Hairdressers Due to Isolated Damage by Cold Wave Liquids is reported by S Borelli and J S Kraft (Univ of Munich) Of 450 young hairdressers who handled c ld wa e liquids daily 315 showed more or less marked, temporary or permanent damage to the skin. I 290 there was marked hyperhidrosis of sudden onset in 237 it co cided with first contact with cold wave liquids. When not exposed (e.g during vacation) these patients showed normal sweat secretion of ha ds Three types of cold wa hyperhidrosis were observed (1) fingers and palms felt wet on touch often showing droplets of sweat (2) fingers and palms seemed slightly swollen and the skin taut, and (3) the latter changes comb ned with spotty erythematou or dark red discoloration with a tendency to fissure with hemorrhagi changes particularly on finger tips nd terdigital webs swelling was well marked.

The pecific effects of th oglycolat on sweat gland erves and vessels or permeabil ty of kin are assumed the ca se of cold wa e hyperhidrosis rather than constitutional factors or damage due to alkalis because hairdressers showed hyperhidrosis only after contact with cold wave liquids Per son dealing only with washing and dyeing of hair but not ha dling cold wa liqu ds showed dry eczema and secondary formation of fissures Testing of palmar secretion re ealed values f aro nd pH 6, ndicati e of sweat. Prognos cases f cold wave hyperhidrosis is good. Whether regular wa h ng w th acid solutions nd use of protective creams ma prevent hyperhidrosis despite continued handling of ld wa liqu ds, cannot yet be determined

► [While report of this type is not unexpected, it is surprising that no such reports of hand involvement, to our knowledge, have appeared elsewhere in the dermatologic literature. This is particularly true for the United States, here cold wav permanents are not only used routinely by beaut parlor operators, but here they ha been widely used in "home

physical appearance hair color and texture and similar fingerprint patterns and iris markings. They first had identical vesicular eruptions on their hands and fingers at age 14 during a period of parental strife. Their eruptions persisted with varying severity for two years despite local medicaments and finally cleared simultaneously after a single superficial x ray treatment.

At 18 one twin (A) worked for more than a year as an automobile mechanic this necessitated exposure of hands to oils and greases that required washing with strong abrasive detergent cleansers. The other twin (B) worked for a telephone company where he handled only clean electric parts and could avoid exposing his hands to strong external irritants. During this period neither experienced skin difficulty

At 19 both entered the Army and were billeted together A continued to handle motor parts which required exposure to oils greases and abrasive detergents, while B continued to handle only clean electric equipment.

A year later for the first time these twins were continuously separated for two months, during which each experienced acute recurrence of his vesicular hand eruption accompanied later by a milder similar eruption on the left foot. Neither knew of the other's eruption until after they were reunited they never wore each other's clothing

On hospitalization physical examination was normal in both except for the essentially nonpruritic skin eruptions. A had an eruption of vesicles in various stages of evolution and involution along the sides of all fingers, the right fifth and the left index finger being most severely affected There were also scattered, crusted and scaly eczematoid patches on the backs of the hands and a multilocular pustule on the sole of the left foot. The eruption on the hands of B was similar though less severe, although he had a more extensive vesiculopustular eruption on the left foot.

Microscopic examinations and cultures of vesicle tops from the hands and feet were negative for fungi in both patients. Unsuccessful attempts were made to isolate a possible and perhaps unknown virus from the vesicle fluid and scrapings from A's lesions by passages on chorioallantoic membranes of embryonated eggs, in suckling mice and in HeLa cell tissue culture (human cervical epidermoid carcinoma) Complement fixation test for herpes simplex virus was positive with A's serum only at minimal dilutions, suggesting old rather than recent infection.

It is suggested that intrinsic factors such as congenitally determined ones, as well as emotional stresses were etiologic essentials The relatively less important factor of exposure to external contact irritants in aggravating the eruption was shown only by the greater severity of the eruption in A That such external irritants were not prime factors in precipitating or causing the eruptions is clear from the facts that in B

Hosp., London) because it may shed some light on this type of dermatitis, which is rarely confined to a nerve lesion.

Woman, 42, who had had headache, failing vision in the right eye and failure of memory and powers of concentration for several years, had a large right temporal meningioma removed. Postoperatively there was complete anesthesia in the area of the right fifth nerve, partial right facial weakness and mild pyramidal signs of the left leg. Deep x-ray therapy to the right sphenoid region followed the surgical excision. Two months after surgery typical lesions of seborrheic dermatitis were noted on the right side of forehead, eyebrow, upper part of cheek and right side of nose, sharply limited at the midline. This area was warmer and strikingly more greasy than the left. The skin lesions cleared after therapy with 1% sulfur and salicylic acid in unguentum aquosum B.P. The skin temperature was higher on the right side of face than the left. There was relative absence of sweating on the right side of face and forehead, but sebum level was twice as great on the right as the left. Many more organisms, primarily Staphylococcus albus, were found on culture of the abnormal side. During the next 18 months she recovered almost completely from the neurologic defects, and no residual seborrheic dermatitis was found.

The relative absence of sweating over the area supplied by the ophthalmic division indicated existence of a sympathetic lesion in addition to a fifth nerve lesion. The abnormality of sweating was not found one year later when the skin lesions had completely disappeared. The following mechanism is suggested to explain the findings in this case. Since both sympathetic and fifth nerve lesions were present, and the eruption was strictly confined to this area, the seborrheic dermatitis must have resulted from a nerve lesion. With recovery from the sympathetic lesion, the skin returned to normal, despite persistence of the fifth nerve lesion. This suggests that the sympathetic lesion played a role in causing the skin disturbance, and it is believed that the sympathetic lesion was in the brain stem. Although there is no evidence to indicate nerve control of sebaceous gland secretion, it is possible that removal of sympathetic control of the blood vessels increases the blood flow to the glands, causing increased activity. There is little evidence to support this thesis, either. The authors are prompted to postulate direct innervation of the sebaceous glands. The holocrine nature of sebaceous secretion indicates this would be akin to a trophic disturbance. It is interesting to observe that the patient showed no general tendency to seborrheic dermatitis

permanents as well. Is it possible that the necessary precaution of wearing rubber gloves while handling these materials has been disregarded by some of those whose hands were damaged?—Eds.]

Hyperhidrosis of Right Hand is described by André Thomas[6] (Paris)

Man was seen first in July 1949 because of writer's cramp. When he was seen again in May 1955 cramping had disappeared almost completely after change of profession, but he complained of persistent sweating of the right hand. The previous condition had originated when in 1943, he was assigned to clerical duties in an Army telegraph unit the latter when he was working as a salesman. He often was self-conscious when he talked to a client or had to shake hands. Sweating also occurred when he cut himself shaving. Examination revealed that, as in many persons with writer's cramp, relaxation was reduced, due to asthenia of antagonistic muscles. Hyperhidrosis of the right palm could be elicited by slight needle pricks to the left palm in a few seconds the right palm became moist. Later, profuse sweating occurred, the fingers became swollen the skin of the involved area grew red and warmer the skin folds thickened and finally all fingers were sweating showing large drops of sweat. The back of the right hand, however remained normal and dry except the periungual and adjacent area of the thumb. The skin of the left hand was completely unchanged sweating redness or changes in temperature did not occur. Neurologic findings were, in general, negative.

Observation of graphospasm and local hyperhidrosis is rather exceptional. Because of sweating limited to the palm of the right hand, elicited by peripheral somatic or psychic stimuli and associated with hyperthermia and redness and because of the restless irritable and emotional character of the patient the condition was classified as "repercussion phenomenon." This includes reactions that are localized in a constitutionally or accidentally sensitized region of the skin or system e.g. vasomotor sudoriferous or pilomotor. These reactions may be elicited by somatic psychic or several stimuli together. Repercussion phenomena occasionally show a familial or hereditary character. They may occur not only within the autonomic nervous system but also in the cerebrospinal system e.g. as so-called involuntary movements (clonic, choreic athetotic movements and fibrillary contractions) caused by excitement.

Unilateral Seborrheic Dermatitis Following Nerve Lesion is reported by F Ray Bettley and R. H Marten[7] (Middlesex

(6) Presse méd. 64 367-369 Mar 3 1956.
(7) A.M.A. Arch. Dermat. 73 110-115 February 1956.

after habitual manipulation such as rubbing light stroking or squeezing the skin or from resting the fingers on the face or the head on the hands. When cystic comedones are pierced sebaceous material escapes occasionally quite odorous. When patients mention an odor beh nd their ears, they usually have these cysts and pressure on them contaminates their fingers. Cystic comedones may also originate from habitual manipulations such as pressure, rubbing pulling or tapping the skin

Comedones and cystic comedo formation from habitual manipulation may be unilateral or bilateral. Only an ear lobe may be n olved, one side of the face or the entire face, chest and back The acts arise from a variety of factors, from an insect bite to x ray therapy of a facial epithelioma. Copy ng of others hab ts and feel ng to see if some trivial trauma is healing ar major factors.

Gaul studied 96 patients with acne in all stages of activity for manipulative habits. Similarly to comedo formation, ac ne f llowed fondl ng rubbing and excoriating the skin The final outcome of manipulating the skin is thickening coarsen ng and roughening Minute hills and valleys crisscross one another as seen n l chenification. Every pilosebaceous orifice becomes a tiny crater Picking the skin induces scarring and changes in pigmentation P cking is often followed by squeezing of the skin The adolescent should be taught that manipulative practices lead to a bad complexion, pimples and scarring

► [The original article is interestingly illustrated Dermatologists traditionally have warned patients with acne to keep their hands way from their faces and not to pick and squeeze, especially in the danger triangle bounded by the nasolabial folds and the upper lip. Fortunately the extreme danger that was associated ith squeezing and spreading infections in this area into the angular vein and in turn to the cavernous sinus has been abolished almost completely since the introduction of antibiotics. The important point once more brought out by Gaul' article is that manipulation of the face can be significant factor in producing new comedones and acne lesions in addition to damaging the skin. The editors are of the opinion, however that permanent damage, such as scarring, is unlikely to occur as result of the usual forms of manipulation practiced by patients, unless (1) there is a particular tendency to scarring, (2) squeezing is done in violent manner or (3) it is accompanied by picking —Eds.]

Knuckle Pads ("Pulvillus Digiti") re reviewed and two cases eported by J Ramos E Silva (Rio de Janeiro)

Case 1 —Man, 29 had varicocele on the left side and for year knuckle pads had appeared on the dorsal aspect of the proximal in-

Am. dermat. et syph. 63 22-32, Jan Feb 954.

and the scalp was free from dandruff Development of seborrheic dermatitis was apparently determined solely by local factors and varied simultaneously with the abnormal greasiness of the skin

► [Another report demonstrating that increased sebaceous secretion can follow in those skin areas in which there has been injury to the innervating nerves. The question of how this change in sebaceous secretion is brought about remains unanswered. It is not necessary to assume neural control of sebaceous secretion to explain the alterations in this case. The changes in the nerve supply merely may have caused a different response of the sebaceous glands in the affected areas to some entirely non-neural (hormonal?) factor.—Eds.]

Observations on Acne Seborrhea and Obesity Stanford Bourne and Allan Jacobs[8] (Wolverhampton) surveyed 2,720 unselected soldiers aged 15-40 to clarify the natural history of acne and its correlation if any with seborrhea, obesity and coloring The incidence and severity of acne was found to be the same in men with all grades of dandruff

Acne is equally common in fair dark and ginger subjects. Dandruff is commonest in ginger men Most acne occurs at age 18-19 and the face is then by far the commonest site Thereafter it disappears from the face most rapidly and the trunk tends to become the predominant site in older men These facts support the theory that comedo formation and acne are related to rudimentary hair growth in immature pilosebaceous complexes following endocrine stimulation, and that acne dies out when the hair is well established as on the beard area

The presence of acne is unrelated to the presence or severity of dandruff The value of shampoos in management of acne is doubtful Treating dandruff may improve some cases, but this seems unlikely A controlled therapeutic test is desirable to justify the considerable effort being expended in treatment of pityriasis capitis During adolescence acne is not related to obesity but males over age 20 with acne tend to be heavier than those without it

► [It should be noted that no women and no males under 15 years of age were included in the authors' series. Many dermatologists have managed their acne cases on the assumption that there is a relation between facial acne and seborrhea capitis. The finding of Bourne and Jacobs throw doubt on the validity of th traditional concept.—Eds.]

Habitual Manipulations in Acne Vulgaris. L. Edward Gaul[9] (Evansville) observed that comedones may develop

(8) Brit. M. J. 1 1268-1270 June 2, 1956
(9) J Indiana M. A. 49 1193-1204 October 1956.

slightly depressed, firm, yellowish patches with telangiectasia and bluish vessels shining through the atrophic epidermis. There were also scleroderma-like, recent, bluish red, cushion-like, ill defined plaques that were swollen and elastic. Minor peripheral scaliness appeared on all lesions (Fig. 23). Histologic study revealed atrophy of the epidermis and papillae. Elastic fibers were rare in the latter and missing in a wide area of the stratum reticulare. In the corium, there were nodular infiltrates of lymphocytes, epithelioid cells, Langhans and foreign body giant cells. Vascular changes con-



Fig. 23.—Granulomatosis disciformis chronica et progressiva (Miescher) of anterior surfaces of both legs. (Courtesy of Goetz, H.: Hautarzt 7:134-141, April, 1956.)

sisted of fibrosis and intima hypertrophy with narrowing of the lumen. Lipid staining gave negative results; necrotic or necrobiotic areas were missing. Padutin® administration (40 units twice weekly) proved highly effective in this case of granulomatosis disciformis.

Case —Woman, 23, had had diabetes since she was 14 and had received insulin (50-70 units daily) ever since. Cutaneous manifestations of necrobiosis lipoidica diabeticorum were first seen in the same year (1946). On examination, both legs revealed large and small firm, atrophic, centrally depressed, dark red or yellowish patches, the periphery of which was covered by loose, coarse, whitish yellowish scales. Histology revealed thickened epidermis and plump rete pegs in the cutis, extending partly into the subcutis, and infiltrates consisting of lymphocytes, histiocytes and plasma cells.

terphalangeal joints of the right middle and left ring fingers. Histologic study revealed epidermal hypertrophy with marked hyperkeratosis, dilatation of papillary vessels, sclerotic, poorly stained fibrosis of the cutis and rarefied elastic fibers.

CASE 2.—Boy 6 had multiple angiomatous nevi of the right upper extremity and chest region. Knuckle pads appeared three years earlier on the dorsum of the proximal interphalangeal joints of the right third, fourth and fifth fingers. Histologic findings corresponded to those in the first case.

Knuckle pads must be differentiated from Heberden's nodes (osteoarticular) systematized fibromas of extensor tendons Duperrat (para articular the overlying skin remaining movable) heloma simplex et annularis Vorner (callosities often appearing on palmar aspects of fingers and even on forearms) and glomus tumor which is bluish and extremely sensitive. Found in 9 4% of various dermatologic observations knuckle pads are assumed to result from formation of a subcutaneous fibroma, caused by local anemia from mechanical tension of the dorsal tissues of the proximal interphalangeal joints This tension is increased in the index and middle fingers which are used so much in grasping or holding objects.

Heredity seems to play an important role. Observations of familial occurrence dominant heredity association with other manifestations of hereditary polyfibromatosis (e.g Dupuytren s contracture) indicate a hereditary factor It may be mentioned that Michelangelo s sculptures of Lorenzo di Medici and his son Giulio display knuckle pads (dominant heredity) Many authors consider knuckle pads to be a *genodermatosis* *The association of knuckle pads* and angiomatous nevi in case 2 lends support to such an assumption

► [The editors are very familiar with one subject with knuckle pads caused by repeated biting of the knuckles over several years. The lesions have persisted, essentially unchanged, for more than 25 years.—Eds.]

Relations between Granulomatosis Disciformis Chronica et Progressiva (Miescher) and Necrobiosis Lipoidica Diabeticorum are discussed by Hans Gotz[2] (Univ of Munich)

CASE 1.—Woman 61 with no family history of tuberculosis, noticed the first skin lesions in 1933 High blood pressure (180/100) had been present for years. Arteriography revealed arteriosclerosis of the femoral artery and its branches. She did not have diabetes. Cutaneous lesions of both legs showed well defined, pigmented,

(2) Hautarzt 7 156-161, April 1956

olism or diabetes have been described. Clinical and histologic resemblance to granuloma annulare suggests similar pathogenesis, particularly because of occasional findings of fat droplets and structural vascular changes. Lesions of necrobiosis maculosa, which resembles necrobiosis lipoidica, histologically show only inflammatory changes. Clinical similarity to granulomatosis disciformis chronica et progressiva (Miescher) is confused because the latter shows a granulomatous infiltrate around the dermal blood vessels, although some association with tuberculosis is suspected. From review of the literature, it cannot be said whether inflammation causes vascular damage or vice versa.

For detection of glycogen in the tissues, Best's ammoniacal carmine was used, with saliva treated controls. A modification of Gomori's technic was used for alkaline phosphatase, using alcohol-fixed tissues and the usual controls. Dermal glycogen deposits were found in all 9 cases of necrobiosis lipoidica studied and in 10 of 12 cases of granuloma annulare, but generally in smaller quantities. Alkaline phosphatase, studied in 15 cases, was found where it is normally present in skin and in areas of early fibrosis. No correlation could be made between occurrence of glycogen and alkaline phosphatase. Every case of necrobiosis lipoidica showed glycogen in necrobiotic foci, independent of fatty change. Vascular lesions were not always present and it seemed unlikely that glycogen deposits are caused by ischemia alone. Presence of glycogen appeared unrelated to connective tissue degeneration, nor was the glycogen in necrobiosis attributed to fibrosis. Fatty change was held due to infiltration from outside the diseased focus. Fat and glycogen might coexist at the same sites, but not necessarily since their means of deposition are different. Alkaline phosphatase studies showed it had no significance peculiar to necrobiosis. Distribution of glycogen in necrobiosis lipoidica and granuloma annulare is consistent with either the inflammatory or the degenerative hypothesis. Necrobiosis lipoidica diabeticorum, necrobiosis in nondiabetics and necrobiosis maculosa are of similar pathogenesis. Granuloma annulare is closer in pathogenesis to necrobiosis lipoidica than to rheumatic diseases.

Sclerosing Lipogranuloma Resulting from Exogenous Lipids is reported in two cases by Victor D. Newcomer

Vessels displayed endothelial hypertrophy often with narrowing of the vessel lumen and thromboses. Collagen was markedly damaged and showed large areas of homogenization and nuclear disintegration elastic fibers were broken or missing Tissues took sudan III stain.

Clinical differential diagnosis between granulomatosis disciformis and necrobiosis lipoidica is difficult often impossible as far as lesions of the legs are concerned cutaneous manifestations on the forehead or backs of the hand resemble granuloma annulare In both granulomatosis and necrobiosis histologic study reveals angiopathy with important vascular changes which in necrobiosis lipoidica together with diabetes mellitus cause inflammation necrosis and finally lipid deposits In granulomatosis disciformis thickening of the vascular walls with homogenization and hypertrophy of the endothelium and even obliteration of the lumen occur In case 1 the underlying causative factor was arteriosclerosis with high blood pressure. Cutaneous manifestations improved after depot padutin* administration. Of primary significance is the absence of diabetes mellitus in cases with histologically proved granulomatosis disciformis. On the other hand, patients with evidence of diabetes mellitus who had suspected or clinically diagnosed necrobiosis lipoidica never showed pathologic signs of granulomatosis disciformis It is quite unlikely that granulomatosis may eventually develop into necrobiosis. It is concluded that in patients with cutaneous lesions suggesting either disease the diagnosis of necrobiosis lipoidica is justified only when diabetes mellitus is manifest or can be ascertained.

► [It would be better to wait until more is known about the mechanism producing both granulomatosis disciformis chronica and necrobiosis lipoidica diabeticorum before restricting the diagnosis of necrobiosis lipoidica diabeticorum to cases in which diabetes mellitus "is manifest or can be ascertained. —Eds.]

Necrobiosis Lipoidica is discussed by P J Hare[2] (Univ College Hosp., London) with particular reference to glycogen and alkaline phosphatase in the lesions The disease was originally described as a complication of diabetes with hard yellow skin plaques showing atrophy and telangiectasia Histologically there are areas of necrobiosis in the corium with extracellular fat droplets and obliterative blood vessel changes are often noted. Cases without abnormal fat metab-

(2) Brit. J Dermat. 67 365-384 November 1955

as a pruritic, lichenoid eruption on the legs consisting of neurodermatitis-like patches, made up of confluent, translucent, pinhead to split-pea sized, pink, red or reddish brown papules. In the secondary type of localized cutaneous amyloidosis, amyloid deposits are found in senile and pigmented verrucae keratomas epitheliomas and cylindromas. Predilection for exposed parts of the body may be due to a secondary process in skin that is already damaged. This type of amyloidosis was found in the following case

Woman, 52, had a facial skin affection for eight years, beginning with asymptomatic, yellow papules on the left cheek, which gradually coalesced to form a yellowish pink, smooth, slightly raised plaque about 2 cm in diameter. There were no symptoms other than disfigurement. Two years after onset she was treated for lupus erythematosus. About seven years later a brownish red patch appeared on the left side of the face, and increased in size.

The patient appeared in perfect health. Results of a general physical examination were essentially normal. Dermatologic examination disclosed two facial lesions. One was a reddish brown, irregular, infiltrated, firm, nontender smooth, raised, slightly dome-shaped plaque about 2.5 cm. in diameter in the center of the left cheek. The second, on the left side of the chin, was similarly colored, infiltrated, smooth patch about 3 cm. in diameter. There were numerous freckles and other pigmented macules over the face, indicating senile degenerative changes. A punch biopsy specimen taken from the margin of the brownish plaque on the chin revealed flattened epidermis. The pathologic changes were limited to the collagen and blood vessels. There were marked edema in the upper cutis, with some distention of the superficial vessel, and a rather diffuse homogenization of collagen fibers, apparently representing a degenerative process which extended also into the blood vessel walls. Congo red stain identified this degenerative substance as amyloid.

The patient did not present any evidence of generalized disease and from the duration of the symptoms absence of amyloid deposits elsewhere the completely negative laboratory findings, primary systematized amyloidosis could be ruled out despite the histologic picture suggesting this disease. Other signs of degenerative skin changes on the face, freckles, wrinkling and seborrheic keratoses would suggest that the amyloid deposits were the end result of degenerative changes

Familial Primary Systemic Amyloidosis Experimental, Genetic and Clinical Study John G Rukavina, Walter D Block and A. C. Curtis[46] (Univ of Michigan) investigated

(46) J Invest. Dermat. 27 11 131 September 1956.

James H Graham Roscoe R. Schaffert and Leo Kaplan[4] (Los Angeles) The term "sclerosing lipogranuloma" has been used for a peculiar granulomatous reaction occurring in subcutaneous fat tissue after injury of various types. It is usually seen in male genital regions as localized swelling which is gradually progressive inflammatory signs are absent The spread suggests a malignant process, especially when regional lymph nodes are involved. Histologically there is disturbance of the architecture of the fat tissue with disintegration of fat cells and formation of globules. Phagocytosis of fat and foreign body giant cells are found. Finally scar tissue containing fat globules and cysts is seen. Fat is altered from normal as shown by difference in staining reactions The disease closely resembles paraffinoma, clinically and histologically

Two cases were seen in white men aged 57 and 38. Both involved the shaft of the penis and followed trauma. Treatment was surgical excision though only partial in the latter case. Both specimens resembled paraffinomas though there was no history of injection in either case. Chemical analysis of the specimen obtained in the first case showed (1) that it contained a triglyceride, (2) that there was unsaturation in the acid portion (3) that the unknown was impure and (4) that the infra red spectrum was close to that of cottonseed oil but mixtures of corn or peanut oil could not be excluded. Subsequent questioning of both patients disclosed injection of some material in the shaft of the penis before onset of lesions These cases are identical with those due to injection of foreign lipids.

From these cases and a review of the literature "sclerosing lipogranuloma" is believed due to exogenous lipids and not to an abnormal self perpetuating endogenous lipoid degenerative process

Localized Cutaneous Amyloidosis is discussed by John M. Siegel[4a] (Sacred Heart Hosp., Allentown Pa) Amyloidosis may be generalized with cutaneous involvement or limited to the skin. The latter may be primary or secondary The primary type has also been called lichen amyloidosis or amyloidosis cutis nodularis et disseminata. It occurs principally

(4) A.M.A. Arch. Dermat. 73:361 372, April, 1956.
(4a) Ibid., pp. 564-567 June, 1956.

pacted or missing. X-ray films of the stomach revealed ptosis, undisturbed mobility and formation of a rigid, enlarged mucosal fold in its upper part. Fasting blood sugar values were slightly increased at times; the blood sugar curve was normal. Electrophoretic examination of the serum proteins disclosed dysproteinemia, with reduced albumin and increased globulin values.

Histologic examination of the tonsil and labial mucosa revealed well defined plaques of vascular connective tissue impregnated with plastic substance, stained pink by eosin, yellow to yellowish brown by van Gieson stain, and colored slightly by Congo red. Elastic fibers were missing within the deposits. The walls of the small vessels, particularly the arterioles, were changed into thick, hyaline rings with compressed intima cells which almost obliterated the lumen. Fat stains showed minimal sudanophilic substances within the deposits.

The elder sister, 25, showed even more cutaneous deposits, but slightly less marked mucosal changes than the younger. Hoarseness existed and dental development was defective. Fasting blood sugar also was normal.

Hyalinosis cutis et mucosae (lipid proteinosis) may occur in several members of a family and show recessive heredity. It is characterized by deposits in the skin, mucous membranes, cranial skull and brain, and is seen in association with defective or delayed dental development, involvement of the gastric mucosa, faulty carbohydrate metabolism and changes in serum proteins.

Recent investigations attribute less importance to the lipid deposits than to faulty protein metabolism with abnormal protein synthesis and formation of heterologous protein (paraprotein) which cannot be split by ferments and which forms a transudate in mesenchymal tissues. Dysproteinemia, as seen in the first case, supports such a hypothesis.

Dyslipoidic Cutaneous Atrophy is described by Fr. Woringer (Strasbourg) and P. Langier[4] (Besançon).

Man, 60, hospitalized because of cancer of the prostate gland, showed cutaneous lesions that had been present for the past 10 years, causing no complaints. The trunk and extremities were mainly involved. The elementary lesion was represented by atrophic, depressed, pinhead- to lentil-sized, round, erythematosquamous, copper-colored macules, partly isolated but often arranged in band-like formations, and partly confluent, which covered in symmetrical distribution nearly a sixth of the skin surface. On the neck, a rhomboid-like group of lesions extended to the sixth dorsal vertebra. From there to the second sacral vertebra and the iliac crest there ... rhomboid, uniform plaque with irregular borders, yellow to

[4] Presse méd. 64:546-547, Mar. 2, 1956.

the pedigree of a family of 66 members for presence or absence of clinical or subclinical inherited primary systemic amyloidosis using clinical laboratory and experimental biochemical methods In 29 evidence of the disease was obtained It is inherited as a dominant character

The bizarre clinical findings in this pedigree, appearing regularly in the third and fourth decades were peripheral neuropathy cardiovascular insufficiency hepatic enlargement and dysfunction unusual ocular manifestations gastrointestinal symptoms and splenomegaly The carpal tunnel syndrome was also encountered.

The usual laboratory procedures proved non pecific and inadequate. In these patients demonstration by free electrophoresis of an atypical peak migrating between the beta and $alpha_2$ globulin areas and demonstration of elevated serum lipoprotein by ultracentrifugation are essentials for the diagnosis They adequately identify the subclinical disease.

The abnormally elevated lipoproteins particularly in the S 25-40 and 20-25 fractions suggest that at least in part, familial primary systemic amyloidosis is an inherited aberrancy in lipoprotein metabolism

Two Cases of Familial Hyalinosis Cutis et Mucosae (Lipid Proteinosis) are reported by Else Hanig and Helmut Kremer[5] (Aachen Germany) in sisters with marked hoarseness and identical mucocutaneous changes since birth

The younger 13 of infantile-hypoplastic type showed vegetative vasomotor lability with marked dermographism, cold, clammy hands and feet, and, since the third year cutaneous lesions. The lesions consisted of yellowish, papular deposits on the face neck, shoulders and limbs which were partly isolated, partly confluent, often linear on the eyelids and reticular on the chin depressions of worm-eaten appearance within the normal skin which under Wood light, did not show any deposits, and roundish scars. The mucosa of the lips, particularly of the lower lip showed indurated, pale yellow plaquelike deposits, and similar papular or nodular deposits on the tongue and its frenulum The tonsils were about the size of a small cherry and firm. Hard plaquelike infiltrations were seen on the arytenoid cartilages and on the left vocal cord, the free margin of which was slightly dentate and contracted, thus interfering with its proper function and producing hoarseness. Dental development was retarded both lateral upper incisors were missing and only a few milk teeth remained. On x ray examination other teeth appeared im-

(5) Hautarzt 6 491-494 November 1955

disturbances, pains and spasms in the hands, feet and upper legs, increasing at higher temperatures and abating at lower (2) edema for years, dependent in type, with no evidence of cardiac renal or blood plasma insufficiency (3) moderately but constantly elevated blood pressure (4) cardiac enlargement, especially the left ventricle, and (5) urinary abnor



Fig. 24.—Left crural fold showing hyperkeratotic lesions of deep purple-red color. (Courtesy of [illegible] R. R., et al. A.M.A. Arch. Dermat. 72:354-361, December 1955.)

malities, with albuminuria, red blood cells, white cells and casts present.

Man, 46, had had persistent edema of the legs. The cutaneous lesions had occurred from age 10 to 18 years. The lesions thereafter had persisted unchanged. Those in the groins were 2 mm. in diameter hyperkeratotic, raised and glistening (Fig 24). The heart was not enlarged, but there was grade 1 apical systolic murmur and grade ankle edema. Grade 3 proteinuria was found, as were some red blood cells, casts and pus cells. X ray of the left hip showed old vascular necrosis of the femoral capital epiphysis. There was ECG evidence of an intraventricular conduction defect. Pathologic section of cutaneous lesion showed thickening of the epidermis and follicular plugging and in the papillary bodies were large vascular

copper red in color The surface was sprinkled with slightly adherent scales that could be *removed by curettage*. Lateral to the plaque were isolated markedly atrophic and depressed lesions in bandlike distribution. Similar disseminated, partially isolated, partially bandlike lesions appeared on arms and forearms, in the gluteal region and anterior aspects of the thighs and legs. Mucosal membranes were free from lesions.

Histology revealed a considerably atrophic epidermis with only two or three layers of cells and a nearly straight lower border. In the cutis elastin fibers were missing and collagen fibers were horizontally arranged. In the superficial parts of the dermis, bandlike infiltrates of epithelioids and giant cells were present, which showed no perivascular distribution No foreign bodies were seen. Examination in polarized light did not reveal doubly refractive bodies. Ziehl Neelsen's stain gave negative results. Prussian blue stain displayed intensive, elective staining of infiltrates but no black granules as in hemosiderosis. Protoplasm of histiocytes showed diffuse blue staining of varying intensity In scarlet red-stained sections, intracellular droplets of lipids were shown, but no xanthomatous cells. These lipids were not doubly refractive McManus reaction exhibited an abundance of fuchsinophil droplets that were not glycogen because Best carmin stain was not reactive in infiltrates.

Laboratory tests showed an average sedimentation rate of 62.5 mm./hour The hemogram revealed 5,260 000 red blood cells and 10 000 white blood cells with 83% neutrophils, 1% eosinophils, 2% monocytes and 14% lymphocytes. Serologic tests for syphilis and skin tests for tuberculosis gave negative results.

Clinically the case presented is different from dermatitis chronica atrophicans anetoderma cutaneous hemosiderosis and purpuric capillaritis Granulomatous changes in the upper corium do not correspond to granulomatosis disciformis chronica (Miescher) Histology indicates faulty lipid metabolism but unfortunately examinations of serum proteins and lipid *metabolism could not be carried out before* the patient died from metastases of the prostate cancer No autopsy was performed

Angiokeratoma Corporis Diffusum is discussed by Robert B Pittelkow Robert R Kierland and Hamilton Montgomery[7] (Mayo Clinic and Found.) The distinctive cutaneous lesions of multiple discrete red purple papules over the knees elbows waist buttocks groins and scrotum have always been noted *before puberty Under the name* cardiovascular renal symptom complex involvement of the internal organs has been summarized as (1) vasomotor

(7) A.M.A. Arch Dermat. 72 556-561 December 1955.

which ere pressed side and often lacerated. Mucinous changes appeared within collagen bundles as fusiform or undulating bandlike deposits and were often seen first at the frayed ends of the collagen bundles. Within the fusiform or stellate accumulations of fibrocytes, there were mucinous collections of rather fine, fibrillar or reticular forms. No mucin formed around the vessels. However it showed in the mucicarmine, trichrome- and toluidine blue-stained sections in collagen bundles, fibrocytes and reticulum cells, and was indicated by metachromatic changes due to polymerization of the dye, particularly of toluidine blue. Elastic fibers



Fig. 23.—Scleromyxedema. Disseminated nodules and coarse folds of thickened, indurated skin on upper chest and shoulder of left side. (Courtesy of Konrad, J. and Winkler A. Arch. klin. u. exper. Dermat. 203:234-242, 1956.)

ex sted only in fragments Abundant argyrophilic gitterfasern indicated degenerated and newly formed collagen.

The kin shows less i duration in scleromyxedema than n scleroderma and can be lifted in coarse folds and shifted on the u derlying ti sues. Occasionally however differential diagnosis of scleroderma (nd sclerodactylia) may be diffi cult especially f observed in conjunction with scleromyx edema In uch case, scleroderma and sclerodactylia l ke changes may be terminal stages of scleromyxedema due to th shrinkage f edematous tissues. The pathogenes s of scleromyxedema is still under consideration. Endocrine distu bances of hypophy ial and pluriglandular origi may play an mportant part. Gottron interpret mucin deposits as n-udates, *resulting* from slowed down circulation and ex tra asation into the tissues, and Tappeiner considers liver

spaces filled with erythrocytes and having thin, intact endothelial walls. There was some vacuolation of muscle bundles.

► [Ruiter (Dermatologica 109:273, 1954) discussed a group of cases with angiokeratoma corporis diffusum in which the altered vascular function apparently depends largely on a disturbance in lipid metabolism.—Eds.]

Scleromyxedema (Arndt-Gottron) Mucinoses of the skin, i.e. cutaneous manifestations caused by deposits of mucin, can be divided into three groups depending on whether hypofunction hyperfunction or no disturbances of the thyroid or other endocrine glands are present. The third group includes lichen myxedematosus with maculopapular lichenoid and urticarial eruptions and scleromyxedema, with papular or lichenoid lesions, together with diffuse thickening and induration of the skin. A case of the latter very rare, type is described by J Konrad and A Winkler[4] (Univ of Innsbruck)

Woman, 57 noticed numerous pinhead-sized lesions on the neck about two years before hospitalization. On admission, she had numerous, closely disseminated pinhead- to millet-sized, slightly raised wax-colored papules, which did not merge into larger patches but often showed moniliform arrangement. The lesions involved chiefly the neck, chest and abdomen, but were also seen on the face scalp, ears (which were thickened) back and arms. The palms, legs, feet, breasts and mucous membranes were free. The skin showed considerable thickening and induration, which, with the masklike configuration of the face somewhat resembled progressive scleroderma. The thickness and induration also caused the formation of coarse solid folds, chiefly on the axillae (Fig 25), cubital fossae and groins (often with limitation of movements of the knees and elbows) Except on the palms and soles, pigmentation was increased, often in the form of spots, particularly on the forearms. Hair was rather scarce on the scalp and lateral parts of the eyebrows. The inguinal and axillary lymph nodes were somewhat enlarged. Clinical examination revealed a slightly enlarged heart, pulmonary emphysema and enlarged thyroid with the trachea dislodged to the right. The liver and spleen were normal

Histologic and histochemical examinations (particularly metachromatic stains, periodic acid Schiff reaction modified by Mc Manus, hyaluronidase) showed deposits of mucin which consisted of acid (hyaluronic acid-containing) and neutral mucopolysaccharides. No mast cells were found, but there were abundant newly formed gitterfasern between accumulations of fusiform cells which separated the fiber bundles of the stratum reticulare and, to a lesser degree, the stratum papillare. Mucin was deposited in the intracellular substance of connective tissue the collagen bundles of

(4) Arch. klin. u. exper Dermat 203 234-273 1956.

turbidity 3+. Total cholesterols were 242.64 mg./100 ml. (esters 151.40 mg. and free cholesterol 91.26 mg.) Electrophoretic serum analysis and determination of protein-bound carbohydrates revealed decrease in alpha globulin and an increase in beta and gamma globulin-bound carbohydrates, with a shift of the normal glucosamine-hexose ratio.

Histologic study showed basal cells rich in melanin the hair follicles were reduced and brought close to the epidermis by underlying mucin deposits hair papillae were often rudimentary and hairs were occasionally twisted and often missing. The sebaceous glands were usually atrophic and their ducts cystic, with an increase of cells. The eccrine sweat glands were rich in glycogen at first, followed by reduction in glycogen and cellular changes, e.g. the formation of granula, occlusion of the lumen and homogenization. The corium showed bandlike deposits of mucin, partly homogeneous, basophilic, fragmented split collagen fibers, and well stained, but fragmented, elastic fibers. Numerous, partly aggregated, young fibroblasts with stellate cellular processes were seen, resembling embryonic connective tissue elements. Capillaries were dilated and showed slight perivascular infiltrates, but near the cutis-subcutis border the hyalin intima and media were noticeably thickened. Muscular elements of the arrectores pilorum were widely separated by mucin deposits.

Histochemical study of mucin deposits (preparation with streptococcic and testicular hyaluronidase, amylase, pectinase, acetylation, bromination and desamination subsequent testing with toluidine blue, colloid sudan, performic acid-Schiff reaction, periodic acid-Schiff reaction, ninhydrin-Schiff reaction and alloxan-Schiff reaction) showed them to consist of a periodic acid-Schiff-positive part containing sugar keratosulfate and metachromatic part containing metachromatic acid mucopolysaccharides. By aid of the alloxan-Schiff and ninhydrin-Schiff reactions, the presence of proteins (composed of alpha amino acids) could be seen. In this instance the mucin deposits consisted of a complex of acid mucopolysaccharides, sugar and proteins. Mucin deposits also contain acid mucopolysaccharides, sugar and proteins but in varying amounts, which tend to show that in various myxodermas different kinds of mucin are deposited in the skin.

A to th pathogenesis of scleromyxedema, formation of pathologic complexes between abnormal serum protein (caused by liver damage) and mucopolysaccharides of the connecti t sue is apparently essential. After precipitation, these complexes correspond to histologically demonstrable mucin deposits. Despite proliferation of fibroblasts, which re responsible for secretion of mucopolysaccharides the latter a e repeatedly changed into mucin (because of faulty serum proteins) which is deposited into the tissues and

damage a factor No vascular changes or liver damage were noted in the case described

Clinical Appearance and Pathogenesis of Scleromyxedema is discussed with reference to histochemical investigation of mucin deposits by E. Keining and O Braun Falco[9] (Univ of Mainz)

Woman 73 first noticed cutaneous changes 1½ years before examination. Later the skin became tense and indurated and showed small lichenoid lesions. On examination, the skin of the entire body except the breasts, groins, axillae and genital region, was lichenified and diffusely thickened appearing like elephant skin. The lesions were millet sized, whitish and partly irregular and often formed fine uneven ridges (Fig 26) The scalp had scanty hair growth the skin was stretched, thin and lichenified. The face



Fig. 26—Scleromyxedema. Area of forehead showing irregular partly lichenoid, partly ridgelike elevations. (Courtesy of Keining, E., and Braun-Falco, O. Acta dermat.-venereol. 36:37 71 1956.)

appeared stiff and masklike, with few wrinkles the indurated skin was scarcely movable and the lips thin and linear On the trunk and extremities, the reddish brown, hyperpigmented skin was somewhat detached from the underlying tissues, but thickened, and could be lifted in broad folds, thereby reducing the motility of the limbs. Neurologic examination revealed marked cerebral arteriosclerosis with consecutive temporary confusion and reduced memory Sclerotic vascular changes were seen in the ocular fundus. Blood sedimentation rate was 23/34 Urinalysis showed 1+ albumin. The bilirubin level was 0 98 mg./100 ml The Takata reaction was 50 mg./100 ml., Weltmann's coagulation band 1 7 and thymol

(9) Acta dermat.-venereol. 36 37 71 1956.

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there is no *real matrix for the formation of new collagen fibers* Collagen fibers are therefore scanty and like elastic fibers imbibed with mucin. Transudation of faulty serum proteins is facilitated by vascular changes and slows down terminal circulation

Cutaneous Elasticity and Hyperelasticity were studied by Francis E. Ellis and William R. Bundick[1] (Univ of Maryland) in 500 patients with various skin disorders using the hand as a *general indicator of hyperelastosis* As an index of hyperelasticity the extensibility of the fifth finger was used. This was measured by having the subject place his extended hand on a flat surface with the forearm parallel to the examining surface, while the examiner extended the fifth finger as far as comfortably possible. The angle of the finger to the flat surface was measured with a protractor As a measure of elasticity the skin on the dorsum of the wrist was elevated between the thumb and the forefinger of the examiner and the relative elasticity was estimated. The skin of the hyperelastic hand feels moderately soft smooth and slightly moist. The feel of the skin resembles that of a baby because practically all infants exhibit hyperelasticity

Increased elasticity of moderate degree occurred in about 18% of patients but tends to decrease with age. Females are more frequently affected than males The condition may be familial This moderate form of elastosis is associated with a soft flexible skin While cutis laxa increases hyperelastosis decreases with age The so-called neurogenic dermatoses were observed less frequently in patients with hyperelastosis.

Parallelism was observed between increased elasticity of the skin and hypermobility of the adjacent joints

With severe elastosis displacement of appendages may develop such as dislocations of shoulders and other joints, but the patients do not tend to have difficulty after surgical procedures *as do the patients with true* Ehlers-Danlos syndrome

Pseudoxanthoma Elasticum and Vascular Disturbances with Special Reference to Case in a 9 Year Old Child. Bo Bafverstedt and Fredrik Lund[2] (Soder jukhuset Stockholm) regard pseudoxanthoma elasticum as a hereditary de-

(1) A.M.A. Arch. Derm 74 22 32 July, 1956.
(2) Acta dermat.-venereol 35 438-445, 1955

generative process in the elastic tissues, manifested mainly by cuta eous and eyeground les ons angioid streaks and circulatory disturbances. Circulatory symptoms are inter mittent claudication cold hands and feet angioid symptoms on effort, dyspnea, fatigue and impaired memory Circula tory signs are feeble pulse in distal parts of extremities, small maximal oscillometric deflections, short and flat oscil lograms abnormally low pulse wave velocities in radial and anterior tibial arteries and changed pulse curves from the arteries of the extremities.

Boy 9 slender but apparently healthy did not race with hi play mates, became irritable and isolated himself but had no pain in the legs. Cutaneous symptoms developed during two years symmetrical small yellow sh gray papules tending to group parallel with the lines of tension commenced on the neck, axillary fold, groin and across the hypogastrium. Slight atrophy and reduced elasticity were evident in the regions most affected. Plethysmography of the fingers and toes showed deformed pulse curves suggestin of altered essel elasticity Arteriography revealed no arterial stenosis, although in this disease, stenosing or obl terative arterial processes occur at an early age, contributing t deformity of the pulse curves.

Pseudoxanthoma elasticum often consists of a triad, of which ascular disease is an mportant component. Cutaneous lesions may occur without angioid streaks and vice ver sa ascular lesio also may conceivably occu alon at least early in the disease In this case vascular lesions may have preceded the cutaneous sympt ms, which had been present only several years before examination. Because of the hereditary fact in this disease, a brother aged 8, was examined for vascular abnormalit es, but none were found. Degenerat e hanges in the ea ly tages of the disease may be localized solely to the vascular elastic tissu

▶ [Mor investigations of this type are highly desirable in pseudoxanthoma elasticum in order to scertain the true extent of the involvement in this disease Shaffer Beerman and Copelan recently reported on two perti nent cases one had idely generalized cutaneous changes with extensi peripheral ascular disease, gangrene of the lower extremities, widespread calcification of the major blood essels and extensive calcinosis of the subcutaneous tissues the other was associated ith Paget disease of the bones —Eds]

Systematized Elastorhexis Pseudoxanthoma Elasticum, Grönblad-Strandberg Syndrome are re iewed by H J Sch ppen a d E Meitl ger St bbe (Un v of Berl n)

M n, 47 had acne when an adolescent, thigh injury with pro-

Deutsche med. Wchnschr 80 1723 1727 Nov 5, 1955

there is no real matrix for the formation of new collagen fibers Collagen fibers are therefore scanty and like elastic fibers imbibed with mucin Transudation of faulty serum proteins is facilitated by vascular changes and slows down terminal circulation

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(2) Acta dermat.-venereol. 35 438-445 1955

and eyes, there was much involvement of the vascular system, such as calcification of the dorsalis pedis, changes of the vascular elastics, as shown by punch biopsy of the spleen and liver and presence of red blood cells in the urine. Pulmonary fibrosis was noted on x-ray, as well as minor osteoporosis and numerous calcifications in soft tissues. The serum cholesterol level was slightly elevated.

The combination of pseudoxanthoma elasticum and angioid streaks, at present called Grönblad-Strandberg syndrome, is a manifestation of systematized elastorhexis, which is a systemic disease of the elastic tissue, showing ocular cutaneous, cardiovascular and visceral signs and symptoms, and has a tendency to occur in families. Heredity (recessive or irregular dominant) mechanical trauma infection and endocrine and metabolic disturbances seem to be contributing factors. Relations to hereditary hemorrhagic telangiectasia, osteitis deformans and Ehlers-Danlos syndrome exist; occasionally concurrence of pseudoxanthoma elasticum and senile colloid degeneration was noted. The authors' patient showed previous trauma and infection but no hereditary factor.

Elastoma Intrapapillare Verruciforme Perforans with Clinical Appearance of Kyrle's Disease is described by G. Miescher[4] (Univ. of Zurich).

Man, 21, when first seen at age 18 had a history of cutaneous changes, present for 11 years and consisting of papulo-verruciform, partly circinate and serpiginous lesions, on the neck and nape of the neck. Five years later irregularly disseminated, pinhead- to pea-sized, firm, bluish red papules were seen on the extensor and lateral surfaces; there were fewer on the inner aspect of the extremities, particularly on the knee and elbow region (Fig. 28). The smallest papules had a smooth, nonscaly surface. Larger lesions were covered by yellowish, horny masses; after they were removed a small, often funnel-shaped, depression appeared. Between papules, the skin was normal but for occasional small, pinkish or slightly pigmented spots, some with minimal atrophy in the center (remnants of involuted or healed papules).

A biopsy specimen was taken from an initial, hardly raised, pinkish, noncornified small papule (2 mm. in diameter) on the upper arm and another from a flat, spherical lesion on the leg, larger than a pinhead and with a horny center. The former specimen showed a massive increase and thickening of elastic fibers in the superficial subpapillary elastic tissue, and particularly in some of the papillae which appeared crammed with masses of elastic fibers. The epithelium was nearly normal. A comparatively insignificant round cell in-

(4) Dermatologica 112:364-315, Apr.-June, 1956.

tracted suppuration, trench fever in 1941-42, and trauma to the right eye in 1944 with gradually deteriorating vision. Since 1935 he had peptic ulcer with adhesions. Skin manifestations started in 1951 and showed typical lesions of pseudoxanthoma elasticum on neck, axillae, lateral parts of trunk and abdomen buttocks, in the inguinal and genital region and on the inner side of each upper thigh. Besides,



Fig. 37.—Stretched skin of lateral part of neck shows pseudoxanthoma elasticum with comedones and false atheromas. (Courtesy of Schuppener, H. J., and Meesmann-Stobbe, E.: Deutsche med. Wchnschr. 80:1723-1727, Nov. 25, 1955.)

lateral parts of the neck showed numerous comedones and a number [illegible] [illegible] red sebum retention cysts [illegible] changes of elastic fibers [illegible] twisted, curled and broken [illegible] dustlike granules. Giant [illegible] degenerated tissue. In Van Gieson stained sections, sporadic basophilic degenerated collagen fibers were found. Ocular changes included angioid streaks and degenerative foci in the macula. Pseudoxanthomatous nodules were found in the fundus changes of the elastica of ocular vessels were suspected. Vision consequently progressively deteriorated. There was considerable visceral involvement. Apart from the integument

and eyes, there was much involvement of the vascular system, such as calcification of the dorsalis pedis, changes of the vascular elastica, as shown by punch biopsy of the spleen and liver and presence of red blood cells in the urine. Pulmonary fibrosis was noted on x-ray as well as minor osteoporosis and numerous calcifications in soft tissues. The serum cholesterol level was slightly elevated.

The combination of pseudoxanthoma elasticum and angioid streaks, at present called Gronblad Strandberg syndrome, is a manifestation of systematized elastorhexis, which is a systemic disease of the elastic tissue showing ocular cutaneous, cardiovascular and visceral signs and symptoms, and has a tendency to occur in families. Heredity (recessi e or irregular dominant) mechanical trauma, in fection and endocrine and metabolic disturbances seem to be contributing factors. R lations to hereditary hem rrhagic telangiectasias, ostitis deformans and Ehlers-Danlos syn drome exist occasionally concurrence of pseudoxanthoma elasticum and senile collo d degeneration was noted. The thors patient showed previous trauma and nfection but no hereditary factor

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[4] Dermatologica 112 304-313, Apr June, 1956.

filtration was noted around papillary vessels and in the subpapillary layer The latter specimen revealed a necrobiotic mass breaking through from the bottom of a pocket like epithelial depression into the corium The necrobiotic mass was enclosed by hyper and para keratotic horny layers and consisted of cellular detritus and dense clusters of elastic fibers which were well stained in the lower parts and hardly recognizable in the more superficial parts of the necro-



Fig 28.—Irregular disseminated primary lesions on lateral aspect of knee (Courtesy of Miescher G Dermatologica 112 306-315 April-June 1956.)

biotic mass. The epidermis showed a marked hyperkeratotic and acanthotic reaction to the break through of necrobiotic elastomatous papillae.

Changes in this case conformed to those of elastoma intrapapillare verruciforme perforans except for differences in localization and spreading Only the neck and nape of the neck were involved and there was no tendency to spreading Involvement of the extremities and irregular dissemination of lesions were characteristic but clinical appearance localization and course strikingly resembled hyperkeratosis

follicularis et parafollicularis in cutem penetrans (Kyrle) Changes of elastic tissue in Kyrle s disease have not been described so far The present case may be only a variant of elastoma intrapapillare erruciforme perforans, with the clinical appearance of Kyrle s disease, or Kyrle s disease may be but a form of elastoma intrapapillare verruciforme perforans.

Acrokeratoelastoidosis, first observed and now described in detail by Oswaldo G Costa[1] (Belo Horizonte, Brazil) mainly in olves the thenar eminence, dorsa of hands and



Fig 29 (Courtesy of Costa, O. G Am Dermat. et syph 83 146-157 Mar.-Apr 1954)

fingers wri ts, shi s ankles, heels and dorsa of feet. Papular keratotic often dyshidrosiform and translucent lesions are seen encased n the epidermis. They are round, oval or polygonal, yellow-white, tender more o less well defined about 1 3 mm. in diameter and often eveal a central crater or umbilication (Fig 29) Occasionally palma -plantar hy

(1) Am dermat. et syph. 83:146-157 Mar Apr 1954.

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Fig 28. Irregular disseminated primary lesions on lateral aspect of knee (Courtesy of Miescher G Dermatologica 112 306-315 April June, 1956.)

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Acrokeratoelastoidosis, first observed and now described in detail by Oswaldo G Costa[5] (Belo Horizonte Brazil) mainly involves the thenar eminence, dorsa of hands and



Fig 29 (Courtesy of Costa, O. G Am Dermat. et syph 83 44-157 Mar Apr 1954)

fingers, wrists shins, ankles, heels and dorsa of feet. Papular keratotic often dyshid osiform a d translucent lesions a e seen encased in the epidermis. They are round, oval o polygonal yellow white tender more or les w ll defined, about 1 3 mm. in diameter and often reveal a central crater or umbilication (Fig 29) Occasionally palmar plantar hy

(5) Am derm. et syph. 83 44 57 Mar Apr 1954.

perkeratosis and hyperhidrosis exist Callous, translucent, firm linear lesions may be seen on dorsa of hands and on the heels Most of these lesions are palpable rather than visible subjective symptoms do not exist.

The ages of five patients observed varied between 18 and 45 years all were Brazilian born female and three were sisters Histologic examination showed hyperkeratosis, hypergranulosis and acanthosis in all. Hypopigmentation was clearly marked in the basal cell layer There was vasodilatation of superficial vessels in the papillary and subpapillary layer perithelial cells were multiplied The collagen showed areas of homogenization but most remarkable were the elastic fibers which were diminished thinned and fragmented. This elastorhexis makes possible differential diagnosis from a number of palmar plantar hyperkeratotic dermatoses, particularly from acrokeratosis verruciformis (Hopf)

Heredity of Keloids Review of Literature and Report of Family with Multiple Keloids in Five Generations. David Bloom[6] (New York Univ Post-Grad. Med School and Skin and Cancer Unit) defines keloid formation as excessive and abnormal fibrous overgrowth of the corium He does not differentiate between spontaneous traumatic or cicatricial keloids He reviewed 31 familial cases of keloids in the literature to which he added the pedigree of an Italian family with 14 affected members in five generations The pedigrees indicate that predisposition to keloids is inherited according to a regular dominant single autosomal mechanism. There is a general local and chronologic predisposition to keloids. In particular smallpox vaccination is a type of trauma which greatly tends to stimulate keloid formation. Others are burns from hot water nitric acid, sulfuric acid, atomic bomb flashes and high frequency coagulation current

CASE 1—Man, 22 had a nervous disease He had had the first keloid on the arm at age 3 after vaccination. Numerous growths had appeared in the ensuing years, preceded by trauma or without apparent cause. These tumors were raised, dime to half-dollar-sized, brownish red, round or dumbbell-shaped and firm and were distributed over the shoulders, upper back, upper and lower extremities and scalp. There was a large keloid on the first toe of the right foot where skin grafting had been performed and one on the donor site of the thigh.

(6) New York J Med. 56.511 518, Feb 15, 1956

CASE 2.—Man, 25 brother of patient 1 in whom the first lesion also developed in early childhood after vaccination, showed a course similar to that of the brother After administration of ACTH flattening of the keloids was noted. One became much smaller when exposed to 300 of x-ray during ACTH therapy

Attention is called to the association of keloids with nervous disorders hyperthyroidism and peptic ulcers Four cases of peptic ulcer in the family described suggests that the same pathogenic factor may cause the tendency to keloids and peptic ulcer Pathogenesis of keloids, like that of peptic ulcer is still obscure. Further study of both may throw light on the causative mechanisms of each and their possible relation

► [It is remarkable that certain cutaneous infections (e.g. smallpox vaccinations) and certain forms of trauma (e.g. high frequency coagulation current) have an especially marked provocative effect for hypertrophic scars —Ed.]

Studies on Nutrition in Far East III. Clinical Indicator Signs of Nutritional Insufficiencies before and after Enrichment of Rice with Synthetic Vitamins. Herbert Pollack[7] (New York Univ Post-Grad. Med. School) found that about 80% of troops of the Chinese Nationalist Army on Formosa during 1954-55 showed ariboflavinosis Half of these had a severe condition and about 20% had the oral-genital syndrome, consisting of scrotal dermatitis, angular stomatitis cheilosis, magenta tongue and nasolabial seborrhea. In the few subjects with optic atrophy skin manifestations were present, but few soldiers with the oral-genital syndrome had optic atrophy

About 30% of troops manifested signs attributable to vitamin A insufficiency and about 20% showed oral pellagroid lesions. It was difficult to interpret follicular keratosis in any and all areas of the body as due entirely to vitamin A deficiency There must be traumatic conditioning factors associated with production of this lesion in some body areas The back and chest were usually the most protected and most sensitive to vitamin A fluctuation.

No signs of protein malnutrition or calcium deficiency were seen in clinical examination. Neurologic screening of this group failed to reveal overt beriberi.

Enrichment of the rice in the diet with synthetic vitamins brought remarkable remission in signs attributable to riboflavin and niacin deficiencies and dietary inclusion of yellow

(7) Metabolism 33 244, May 1956

sweet potatoes improved the vitamin A status The suggested daily vitamin supplement for these rice-eating people is 1 mg thiamine 3 mg riboflavin 15 mg niacin 5 000 units carotene or 3 000 units vitamin A and 20 mg or more vitamin C

► [These findings indicate that where certain dermatoses are the result of vitamin deficiencies, relatively small daily doses of vitamins will correct the situation. It has been thought for some time that when large doses of vitamins are required, for example 50,000 units and more of vitamin A for keratosis follicularis and ichthyosis, 50,000 units and more of vitamin D² for certain tuberculoderma, and so on, these compounds act via mechanisms other than relieving an avitaminosis. We have yet to see a patient in our private practices with nasolabial dermatitis, scrotal dermatitis, angular stomatitis, etc., whose eruption cleared due to systemic therapy with riboflavin.—Eds.]

Cutaneous Mucointestinal Syndrome Study of Degos Malignant Atrophic Papulosis. G B Cottini and S D Randazzo[*] (Univ of Catania) report a case.

Man, 22, had lesions on the cheeks, forehead, trunk, extremities and genitals, secondary to a vesicopustular lesion that had appeared six years earlier on the left corner of the mouth. The primary lesion became ulcerous and extended to the mucosa of the oral cavity and, much later to the preputial mucosa. The skin lesions were lentil sized and superficial with the papules undergoing apparent atrophy (Fig 30) In the phase of central atrophy and peripheral pigmentation, they tended to become vesicopustular and ulcerous, and then to regress and cicatrize. Cultures were positive for Staphylococcus aureus and Streptococcus viridans. Histologic studies revealed epithelial atrophy absence of inflammatory dermal infiltration and vascular capillary impairment with a slight cellular reaction near the lesions. Topical treatment and streptococcus vaccine given intramuscularly subcutaneously and intravenously were without effect. Abscesses that developed at the site of subcutaneous and intramuscular injections were treated by aspirating the fluid and introducing a penicillin solution. Vitamin B_2 massive doses of vitamin C intravenously and calcium and tetracycline for about one month had no effect on the skin lesions those in the oral cavity and genital mucosa healed completely and the general condition improved. One month after discharge he had a sudden profuse enterorrhagia preceded by diffuse peritoniti -like pain and accompanied by high fever After intense pen cillin and streptomycin therapy and blood tran fu ions for one week, the attack ubsi led lea ng him severely a thenic and anemic. The skin lesion rema ned unchanged, as did the healed mucosal lesions. Diagnosi n difficult Degos Delort Tricot disease wa suggested by the clinical erythematous, papular skin lesions, histologic changes, chronic course with good general condition and no grave signs of concomitant o causal nfection tates, and the

(*) Minerva dermat. 31 1-9 January 1956.



Fig 38—Characteristic papulosquamous aspect of cutaneous lesions (illustrative group on anteromedial region of right thigh) Arrow points to typical, deliberate element (Courtesy of Cottini, G B and Randazzo, S D Minerva dermat. 31:1 9 January 1954)

sudden enterorrhagia, which was not fatal, however Against this diagnosis were concurrent involvement of mucosa, the fact that the enterorrhagia was not fatal and the unusual chronic course of the cutaneous and mucous membrane involvement before the abdominal attack.

► [Many of the clinical and histologic features of the dermatosis presented by this patient do not seem to fit in with the original description of malignant atrophic papulosis by Degos, Delort and Tricot in 1942 and by Degos in 1952 (Ann dermat. et syph 79 410, 1952) For example, the thromboses with hyaline degeneration of the vessel walls and the striking absence of inflammatory infiltrate were not present in the case of Cottini and Randazzo

In the latter case despite the positive cultures for Staph. aureus and Str viridans which could have been contaminants or secondary invaders, there are features also which might possibly suggest virus etiology These are the involvement of both mucous membranes and skin, erosopapulopustular lesions which terminate in atrophic changes in the skin and failure to respond to wide spectrum antibiotics —Eds]

Aphthosis is discussed by Helen Ollendorff Curth (Columbia Univ) In addition to the trisyndrome of recurrent uveitis with hypopyon, aphthous lesions of the oral mucosa and genital ulcerations, various other changes have been observed in Behçet disease, which is considered but a part

(9) Ann dermat et syph 81 136-4 Mar-Apr 1954

of aphthosis Similarly ulcus vulvae acutum (Lipschütz) and recurrent periadenitis mucosae necrotica (Sutton) are assumed to correspond to genital and buccal lesions of the disease the latter involve the esophagus and duodenum. Recurrent uveitis with hypopyon is often preceded by vascular retinal changes. Cutaneous necroses and ulcerations are occasionally extensive, particularly in males recurrences of these lesions in old scars apparently prove the absence of local immunity

In about 7% of patients with rapid development of lesions in the oral cavity genital region and eyes the central nervous system was involved showing signs and symptoms similar to those of multiple sclerosis euphoria and mental deterioration scanning speech ataxia of upper and lower extremities uni or bilateral paralysis of the 3d, 4th 6th and 7th cranial nerves nystagmus and Babinski s phenomenon. Cerebrospinal fluid contained between a few and 300 cellular elements and up to 189 mg/100 ml proteins. The EEGs displayed diffuse anomalies Patients with central nervous system involvement usually live for years In instances in which autopsies were performed cellular infiltrations of the meninges and degenerative changes of the ganglions, particularly of the basal nuclei accompanied by slight glial proliferation were revealed. In the mesocephalic regions enormous cell infiltration by polymorphous nuclei and a few hemorrhages existed

In aphthosis small lesions of the erythema nodosum type may occur on legs and arm which histologically show vascularities with thrombosis and hemorrhage of adjacent connective tissue in the subpapillary middle and deeper cutis. Thrombophlebitis and recurrent phlebitis migrans were also observed Vascular and perivascular change occur early in the disease at a time when the epidermis is still intact they represent initial changes whereas ulcerations are secondary Ocular lesions occur oftener in men and buccal and genital lesions oftener in women The etiologic factor—virus or ultravirus—has not been discovered Therapeutically blood transfusions and injections of gamma globulin are recommended rather than the use of cortisone

The term aphthosis is preferred to Behçet s triad because apart from the three classic manifestation other cutaneous,

vascular and nerve lesions may occur thus characterizing aphthosis as a generalized disease with a sometimes fatal end. Histologic stud es prove the etiologic significance of vascular changes.

Neurohistologic Differential Diagnosis of Prurigo Nodularis Hyde and Other Types of Circumscribed Lichenification were studied by W Thies[1] (Univ of Munich) by comparing histologic findings of nodular lesions of four cases of prurigo nodularis Hyde with those of one case each of neurodermatitis gigantea and neurodermatitis nodularis and five cases of neurodermatitis chronica circumscripta.

In the prurigo nodularis group apart from characteristic epidermal changes (hyper and parakeratosis, hypergranulosis, hyperacanthosis) marked alterations were seen in the corium (1) Infiltrates consisting of round cells, histiocytes, fibroblasts, a few mast cells and eosinophils (in one case also numerous polynuclears) extended down to the sweat gland region in nodular bandl ke or perivascular arrangement. (2) Vascularization was abundant within infiltrates, with dilated capillaries often showing convolution and budding swollen endothelial cells and occasional thrombosis of vessel lumen. (3) There was remarkable massing in the corium of nerve elements large nerve trunks enclosed by infiltrates or situated at the periphery of nodular infiltrates were mostly of mixed nature contain ng thick, medullated and fine reticular nonmedullated fibrils. Oval Schwann nuclei, rich in chromatin and therefore darkly stained, were considerably increased in number No proliferative tendency of cutaneous nerves was seen outside prurigo nodularis nodules n adjacent normal ski W thin the nodules between cellular infiltrates a marked increase of interstitial cells and unusual density of plasma strands existed, with nerve fibrils bowing in the darker stained protoplasmic syncytia, with irregularly spread acuoles

Si ce proliferati e tendency of sympathetic terminal networks was not seen in normal skin in prurigo nodularis and was not observed in the group of seven neurodermatitis cases (nodularis gigantea and circumscripta chron ca) it was considered characterist c These pathologic changes of the sympathet c nervous system, however together w th increase of

(1) Arch. klin. exper. Dermat. 201 539-553, 1955.

cellular and fibrillar components were not believed to be the primary alteration It was assumed that the same pathogenic cause elicits simultaneously the vascular and nerve changes and the massive inflammatory infiltration

Lichen Sclerosus et Atrophicus in Childhood. This condition has been reported mainly in girls. The appearance of the lesions is the same as in the adult but location is less varied. The vulva and perianal area are usually the sole sites af



Fig 31—Lichen sclerosus et atrophicus (Courtesy of Ditkowsky S. P et al A.M.A. J Dis. Child. 91 52 54 January 1956.)

fected the eruption having a figure-eight like configuration The tissues especially about the clitoris and perineum, are swollen white and excoriated Tiny hemorrhages from scratching may be present At onset subjective symptoms may be absent and the eruption found only on general physical examination

Sol P Ditkowsky Alfred B Falk Norman Baker and Morton Schaffner[2] report on eight white girls aged 3½-6½ Diagnoses were based on clinical findings confirmed by microscopy of dermal specimens removed from the affected vulval sites

(2) A.M A J Dis. Child. 91:52 54 January 1956.

Girl, 4, was seen because of vaginal discharge and itching about the genitals. Examination revealed white plaquelike lesions over the vulva (Fig 31). Local therapy was ineffective and the lesions extended. Two years later spontaneous improvement began. At age 12, there were no subjective complaints, though slight residual disease remained about the clitoris.

Microscopic studies consistently revealed hyperkeratosis, keratotic plugging and atrophy of the epidermal prickle cell layer with edema of the upper corium and a midzone inflammatory infiltrate.

The cause of this disease is unknown. Treatment is unsatisfactory. Avoidance of trauma seems to prevent extension and possibly aids earlier involution in some patients. Febrile states, especially the exanthemas, aggravate local findings. In the child, improvement is slow, gradual and spontaneous, taking months or years to achieve cure. Corticosteroids seem most useful in alleviating subjective discomfort.

► [It is fortunate that the prognosis in children is so much better than in adults. We have not seen any cases of lichen sclerosus et atrophicus in middle-aged or older women which cleared spontaneously even over a period of many years' observation.—Eds.]

Erythema Annulare Centrifugum was observed in 11 women and 1 man by Anna Nordenskjöld and Fredrik Wahlgren[1] (Stockholm). The disease begins with erythematous papules, which form annular or polycyclic patches with infiltrated marginal zones (Fig 32). The patches extend peripherally while the central area shows healing. The lesions are bluish red in the center and red at the circumference. The disease occurs equally often in both sexes and in all age groups. There is some predilection for the neck, arms, legs and thighs though other regions may be affected. Itching seldom occurs. Treatment of all types is generally ineffective. Spontaneous subsidence is common though recurrences are frequent. The disease occurs spontaneously in seemingly healthy people, or it may be superimposed on some internal disease, e.g., syphilis, tuberculosis, malignant tumors, cardiac and metabolic abnormalities, blood dyscrasias and polyarthritis. Id reactions to fungous infections of the feet have also been noted. Granuloma annulare and ringworm should be considered in the differential diagnosis.

The 12 cases were essentially similar clinically and pathologically. In most patients duration of the lesions was short

(1) Acta dermat.-venereol. 35: 283-291, 1955.

—one to two months—though in several instances they lasted many years Results of laboratory examinations were within normal limits in all patients. Heavy metals, antibiotics and antihistamines were ineffectual in treatment. Microscopic examination usually showed no changes in the epidermis or superficial portion of the corium There were aggregations of inflammatory cells chiefly lymphocytes, surrounding the



Fig 32.—Lesion of erythema annulare centrifugum showing stationary nonitching erythema one patch, bluish red in center with red, infiltrated margin of separate papules. Vascular changes are absent. (Courtesy of Nordenskjöld, A., and Wahlgren, F Acta dermat -venereol. 15:281 291, 1935.)

blood vessels and appendages in the intermediate and deep layers of the corium

Lupus erythematosus differs from erythema annulare centrifugum in that there are epidermal changes, degenerative alterations of the collagen strands of corium and localization of the inflammatory cell nests Chronic lymphatic leukemia shows larger and more compact nodular masses of lymphocytes and the hematologic findings are diagnostic. In lymphadenosis benigna cutis (Bafverstedt s disease) islets of lymphoid tissue may be so highly differentiated as to show follicular structure with germinal centers in the corium.

Erythema annulare centrifugum appears to be more common than has been supposed.

► [It appears remarkable that some uthors (see following article) are able to find "cause" for each case of erythema annulare centrifugum, hile others cannot find the cause even in single case among series of 12 patients.—Ed]

Histopathogenesis of Erythema Annulare Centrifugum is described by F Nodl[4] (Univ of Gottingen)

Man, 28, and woman, 29 showed typical cutaneous manifestations of erythema annulare centrifugum which, after six months duration,



Fig. 33.—Man, 28, with erythema annulare centrifugum. (Courtesy of Nödl, F Arch. klin. u. exper. Dermat. 203 407-423, 1956.)

involved nearly the entire skin surface except the outermost areas of the buttocks (Fig 33) I these patients, focal infections of tonsils and teeth, respectively existed After infections were cleared by antibiotics, the resistant skin lesions disappeared almost completely

Extensive histologic in estigations revealed marked tissue eosinophilia with swarming of eosinophilic granules marked edema, homogenization of connective tissue and sometimes

(4) Arch klin exper. Dermat 203 407-423 1956.

with subcorneal vesicles in the epidermis associated with changes of vascular walls particularly of arterioles characterizing the erythema as an allergic process. Eosinophilic granules consist of a mixture of proteins and lipids, also containing iron and phosphorus Their acidophilic properties are due to basic histons Nuclei of eosinophils are sensitive to desoxyribonuclease-like cells of the lymphatic system, and like neutrophils the eosinophilic cells possess a marked affinity to sudan black B The swarming out of eosinophilic granules is but a defensive action aimed at fixation and elimination of antigens by aid of the lipids of the eosinophilic granules Conversion and precipitation of lipids occur within the tissues, lipid deposits appear in damaged vessels, due to histotoxic hypoxidosis Concomitant with shift of lipids in tissues are reductions of some fractions of serum lipids which, after involution of cutaneous lesions return to normal.

Unusual proliferation of eosinophils in the bone marrow and loss of lipoprotein granules at the periphery are the cause of transitory diminution of serum lipids The sudden increase of tissue eosinophilia, the rapid influx of eosinophils, like disturbances of circulation and permeability (edema, homogenization of connective tissue subcorneal vesicles) may be assumed to be due to nerve and possibly cellular or humoral factors

Aside from the tissue eosinophilia type of erythema annulare centrifugum there also exists a tissue lymphatic type caused probably by a more uniform prolonged flow of antigens which distinguishes it from the type described, and which may be due to sudden inundation with allergens, increased virulence of the causative micro-organism or altered response of the patient

► [The evidence put forward by the author in favor of the role of focal infection in tonsils and teeth in the causation of erythema annulare centrifugum is not very convincing Even if the antibiotic medication resulted in clearing of the eruption, this by no means constitutes conclusive proof that the effect was achieved via control of the infectious foci in the tonsils and teeth.—Eds.]

Origin of Nevus Cells and Genetic Relation of Pigment Cell Nevus, Blue Nevus and Recklinghausen's Phacomatosis are discussed by Taro Kawamura[5] (Univ of Kanazawa Japan) Various theories exist as to the origin of nevus cells

(5) Hautarzt 7 7 14 January 1 54.

Nevus cells have been thought to trickle off at the epidermal dermal junction (theory of "dropping off") to derive from undifferentiated mesenchymal elements (Maximow) or from mother cells (epithelial fiber mother cells) Masson assumed the presence in the epidermis and cutis of a nervous cellular system and that the pigmented nevu is a growth arising from it recently he believed nevus cells to originate from melanoblasts and from Schwann s syncytium. Dropping off" takes place not only at the epidermal-dermal junction but also at the epithelial borders of hair follicles and sweat ducts It does not a priori, exclude autochthonous nevus cell formation in the corium Regarding the latter fact, several indications were observed. Close relations were found, histologically between nevus cells and Schwann elements. Also there were findings of fibres naeviques (Masson) which stain like Schwann s syncytium and were seen in pigmented nevi furthermore the presence was noted of so-called chromatotrope lipids and lipoproteins that show metachromatic staining with thionine and were found in normal nerve fibers as well as in nevu tissues finally there was occurrence in nevus cell nests of argyrophil fibril which are due to a mesenchymal reaction All these fact point to a close relation between nevus cells and Schwann s syncytium, both cell types showing transitions from one to another

Generally nevus cells in the superficial parts of pigmented nevi are related to melanoblast In the deeper part to the Schwann syncytium Pigmented nevi however should not be considered as mixed tumors composed of melanoblasts and Schwann elements Rather it is assumed that the aried nevus cells originate from abnormal cells of the neural crest that from the beginning were dysontogenetic This holds good also of Recklinghausen phacomatosis. In the latter cellular elements develop either toward melanoblasts or toward syncytium cells tumor formation consisting of both types combined is very rare

Assuming that melanoblasts and Schwann s syncytium originate from the neural crest Kawamura concludes, in interpreting pigmented nevus, typical and atypical blue nevus and Recklinghausen s phacomatosis as cutaneous disorders, that dysontogenetic elements of the neural crest are of pathogenetic significance.

Cactus Granulomas of Skin Report of a Case is made by Louis H Winer and Robert H Zeilenga[6] (Univ of California Los Angeles) ... foreign body g ... spine a barbe ... s ... pe e ra es the skin more easily than spicules of glass

Woman, 47 picked a ball-like fruit from a cholla cactus, the sharp bristles of which pierced the dorsum and web of her right thumb and index finger and wrist. Within 72 hours, the right hand became swollen and remained so for three weeks. In the involved areas were numerous red, slightly elevated globular papules, 2-4 mm. in diameter with a central punctum from which protruded a short, stubby hairlike bristle (Fig 34) Clinically the lesions resembled granu-



Fig 34.—Close-up view of lesions on back of right thumb and index finger (Courtesy of Winer L. H., and Zeilenga, R. H. A.M.A. Arch. Dermat. 72:564-569 December 1955)

loma annulare Histologic sections showed hyperkeratosis and mild acanthosis. There were numerous foci of epithelioid cells surrounded by giant cells. Elastic fibers (Verhoeff's stain) were absent from the upper and midcutis, but were fragmented in the lower cutis. There were clear spaces in the giant cells on hematoxylin-eosin staining which were bright red, sharply marginated spicules as seen with Hotchkiss McManus stain.

The chief symptoms in all cases reported were an immediate burning sensation redness and swelling which remained one to three days if the spines were removed. Local tissue necrosis without suppuration or lymphangitis accounts for the spontaneous extrusion of the spines Lesions caused by cactus that have been reported are suppurative lesions, ankylosis of interphalangeal joints nerve paralysis verrucous lesions and cystic osteolytic lesions of bone The red

(6) A.M.A. Arch. Dermat. 72 564-569 December 1955.

reaction to Hotchkiss-McManus stain indicates that cactus spines contain a polysaccharide similar to that seen in wood.

► [The extent of the various types of lesions which are reported due to these cactus bristles is indeed amazing. Of course it would be interesting to know more about the chemical nature of the substances which undoubtedly are liberated by the bristle. Fortunately it should not be difficult to establish the diagnosis for this eruption—one is unlikely to forget contact with such a plant.—Eds.]

Puzzling Persistent Penile Plaques, in contrast to the common acute, subacute, recurrent and chronic lesions of the penis, may be exceedingly difficult to diagnose and treat, according to Marion B. Sulzberger, Victor H. Witten and John A. Hunt (New York Univ. Post-Grad. Med. School and Skin and Cancer Unit).

Lichen planus of the penis is typically seen as polygonal papules, discrete or coalescent in linear or annular configuration, that are bluish red or dull crimson. Inflammation and induration complicate the diagnosis but associated signs of lichen planus usually suggest it. Areas of hyperpigmentation are common sequelae, depigmentation rare.

Psoriasis vulgaris of the glans is well marginated, erythematous and covered with a thin scale, the removal of which will produce minute bleeding points (Auspitz sign). Other signs of psoriasis including pitting of the nails are usually present. Arthritis may be associated in as high as 25% of the cases. The histopathology is characteristic. Response to local therapy is usually prompt.

Distinctive exudative discoid and lichenoid chronic dermatosis is characterized by four phases in which there may be some overlapping and concurrent appearance of lesions of different types: (1) an exudative and discoid phase, (2) a lichenoid phase, (3) an infiltrative phase and (4) an urticarial phase. The infiltrated plaques are sharply defined, violaceous, extremely pruritic and similar to the premycotic stage of mycosis fungoides. The penile lesion (Fig. 35) is a regular feature of this disease; the plaque may persist long after other lesions have disappeared. The histopathologic picture, while not diagnostic, has recognizable features. There are some parakeratosis and irregular acanthosis in the epidermis; suprapapillary plates are thin; exocytosis and a few halinized and dyskeratotic cells are present. The in-

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7) A.M.A. Arch. Dermat. 73: 93-109, February, 1956.

flammatory infiltrate of the corium varies from pure plasmocytes to combinations of small round cells histiocytes and leukocytes. Edema is commonly present Both clinical and pathologic diagnoses may be exceedingly difficult.

Erythroplasia of Queyrat is a well defined bright red, persistent plaque with a shiny often moist surface The lesions grow slowly by peripheral extensions The plaque appears on the glans encircles it and may extend over the sulcus and corona to the shaft In the past penile lesions with out and with the dyskeratotic changes of Bowen's disease have been diagnosed as erythroplasia In America no cases diagnosed as erythroplasia have been known to become cancer The authors are of the opinion that the cases which remain benign both clinically and histologically are not erythroplasia Blau and Hyman assert that histologically bowenoid features must be present to make the diagnosis. The epidermal elements show cellular and nuclear pleomorphism multinucleate cells mitotic figures intracellular edema and

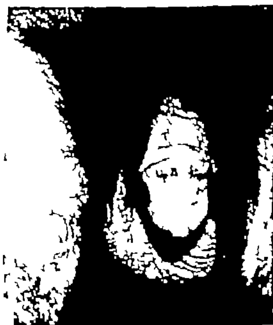


Fig 35.—Distinctive exudative discoid and lichenoid chronic dermatosis (Sulzberger and Garbe) (Courtesy of Sulzberger M B, et al J A M A Arch Dermat 73 101 109 February 1956)

dyskeratotic forms of the grain and corps ronds types. It is of particular interest that in 62 American cases, reported as erythroplasia, only 16 patients showed histologic evidence of malignancy. Of these 13 were uncircumcised.

It is concluded that persistent penile plaques without bowenoid changes are not erythroplasia but are some other dermatosis, probably a phase of exudative discoid and lichenoid chronic dermatosis, especially when they show favorable response to steroid therapy. The importance of careful history taking regarding possible associated lesions and the necessity of thorough examination of the skin are stressed.

[It is worth emphasizing that erythroplasia of Queyrat occurs almost exclusively in the uncircumcised. It should be re-emphasized that other forms of carcinoma of the glans also occur predominantly in the uncircumcised and that the incidence of carcinoma of the cervix is much lower in religious groups where circumcision is a custom.—Eds.]

Increased Familial Incidence of Pitting of Nails in Alopecia Areata is reported by G. Klingmüller and E. Rech[8] (Univ. of Bonn).

Boy, 6, had had alopecia for two years. On examination he was clinically neurologically and psychologically normal but had complete loss of hair (scalp, eyebrows, eyelashes and lanugo). The scalp was hypotonic, excessively oily and, on compression, showed a rhomboid pattern. Pitting of the nails was more marked on the fingers than on the toes. His sister, aged 8, had fully grown scalp hair but showed pitting of all finger-nails. The mother, 34, had dry strawlike hair due to permanent waves, which was otherwise normal dark hair, but the eyebrows were rather scanty in their lateral parts. Pitting of nails was apparent. When questioned about her family she stated that she as well as two elder brothers had had alopecia areata.

Pitting of the nails is frequently observed in psoriasis, seborrheic dermatitis, eczema, lichen planus of the nail root, occasionally in some ectodermal defects and in alopecia areata. In the last instance there is often splitting of the free edges of the nail. Investigation by the author revealed that 36 of 553 school children with skin diseases (6.5%) and 41 of 62 patients with alopecia areata (66%) showed pitting of the nails. The marked difference between the occurrence of pitted nails in alopecia areata in normal persons and in patients with skin diseases strongly supports the hypothesis that alopecia areata with pitting of nails is a real syndrome of a pathogenetically uniform disease. Increased familial incidence

(8) Arch. klin. u. exper. Dermat. 201: 574-580, 1955.

may be observed not only in alopecia areata but also in the occurrence of alopecia areata with pitting of nails.

► [An interesting observation, to our knowledge, not previously reported. The coincident appearance of alopecia areata and pitting of the nails is strong evidence that the disease is not as strictly localized as has been assumed, hitherto clinical search usually was limited to the patchy loss of scalp and other hair.—Eds.]

Alopecia Areata. Hairgrowth in certain body areas, e.g. axillary and pubic hair hair on the trunk and extremities, beard and eyebrows is unquestionably subject to hormone influences but it has not yet been demonstrated whether endocrine factors influence cranial hair Although administration of testosterone may cause hair loss on the forehead and cranial apex a ring of hair remains on the occipital part of the skull and above the ears. Alopecia areata often affects cranial hair and may spread over the entire skull Furthermore it may lead to lack of hair over the entire body surface (alopecia universalis)

J C Seelen L. A M Stolte, J H J Bakker and E. Verboom[9] (Univ of Utrecht) made endocrine studies on 12 patients with alopecia areata. All had normal ovulatory cycles. The BMR was slightly increased in a few Strikingly the 17 ketosteroid excretion was low to low normal in many patients

The low 17 ketosteroid excretion and absence of increase following corticotropin intravenously in one patient suggested a disturbance in adrenocortical function in some cases of alopecia areata The findings available do not warrant the conclusion however that this functional disorder is the cause of the alopecia. It should be borne in mind that marked adrenocortical dysfunction as in Addison s disease is not accompanied by hair loss in the male and only by loss of axillary and pubic hair in the female

In one patient five weekly intramuscular injections of 25 mg progesterone crystals arrested hair loss hair color changed and hair growth occurred on the bald patches. Progesterone was later replaced by 17 hydroxyprogesterone 65 mg /week intramuscularly When the dose of the latter drug was reduced to 65 mg every 14 days loss of hair recurred. It was again arrested when the greater dosage was resumed. Similar results were achieved with progesterone in another

(9) Acta endocrinol. 21:60-71, September 1956.

patient. In both these patients the hair loss was post partum

► [We, too, have found that the most thorough endocrinologic work-up only in the rarest instances turns up any abnormalities that might account for thinning of the scalp hair in otherwise healthy women. This is true also for alopecia areata and alopecia universalis.

However in agreement with the report of Seelen et al., Orentreich at the New York Skin and Cancer Unit has found low normal or abnormally low 17-ketosteroids in number of patients with alopecia areata and alopecia universalis.—Eds.]

Delayed and Persistent Dermographism was observed in an unusual case reported by E. H. Hermans Sr. E. G. Hermans, Jr. and J. P. Nater (Rotterdam)

Man, 41 for eight years had swelling on any part of the body



Fig. 36.—Maximal reaction, seven hours after trauma. (Courtesy of Hermans, E. H. Sr. et al. Nederl. tijdschr. geneesk. 98:324-330, Feb. 1954.)

exposed to trauma. The lumps itched severely and lasted about 24 hours. Various treatments, including injections of the patient own blood, calcium injections and antihistamines were without effect. General physical and neurologic examinations revealed no abnormalities. Results of blood and urine examinations (including test for

( ) Nederl. tijdschr. geneesk. 100:324-330, Feb. 4, 1956.

porphyrin) and a serologic test were negative. The stool showed no parasites (the patient had had amebic dysentery in a Japanese prison camp)

Dermographic signs were elicited when the skin and mucosa were stroked vigorously with a tongue depressor Erythema developed immediately 3 minutes later urticaria appeared and was maximal in 15 minutes, then receded. The reaction increased again four hours later and reached a maximum after six to eight hours (Fig 36) After 14 hours the swelling was considerably decreased, and at 24 hours only slight erythema was evident.

Intradermal injections of various antihistamines, heparin, acetylcholine or histamine did not inhibit the reaction. The first impression was that an injection of hydrocortisone reduced the reaction, but treatment with cortisone (100 mg./day) did not prevent the recondition. Intracutaneous injection of epinephrine inhibited the reaction. It was not inhibited by previous iontophoresis with various antihistamines indicating that histamine probably was not a factor

When congestion or ischemia was produced in the arm by application of a pressure band, stroking the skin with a tongue depressor caused no dermographism for four hours. Then the reaction developed and lasted about 20 hours. Passive transfer of the patient's serum (Prausnitz Kustner method) did not cause a dermographic reaction in the recipient A skin biopsy specimen taken during a dermographic reaction showed no abnormal increase of mast cells.

Similar cases in the literature have been termed pressure urticaria "mechanical late urticaria" and delayed and persistent dermographism " Since the condition is not urticaria but a type of dermographism the authors prefer to call it delayed and persistent dermographism or dermographia tarda et perstans

► [In a similar case seen by us the passive transfer test also was negative. —Eds.]

Bone Lesions in Urticaria Pigmentosa Report of a Central Registry on Skeletal X ray Survey F Sagher and S Schorr[2] (Hadassah Univ Hosp Jerusalem) describe two entirely different forms of bone lesions detected in 19 of 52 patients with urticaria pigmentosa. The generalized type included generalized cystic osteoporosis of the ribs, with a thickening of bony trabeculae stippling of the bony structure in the skull and thickening of the skull tables and generalized sclerosis of the pelvic bone and vertebrae The bony pattern was consistent predominantly with osteosclerosis. The localized type included calcified deposits and decalcified areas of various size in the humerus radius femur skull and shoulder

(2) J Invest. Dermat. 26:431-434 June, 1956

There was no sex preponderance. All four pat ents with urticaria pigmentosa and generalized bone lesions and both patients with mast cell disorders other than urticaria pig mentosa were adults Among the 15 patients with localized bony changes, 3 were children aged 3½ 5½ and 13 years In one patient the nature of the bone lesions with generalized osteosclerosis was ascertained at autopsy Mast cell aggregates were detected in the affected bones

These findings indicate that the tissue mast cell has affin ity for the bone marrow causing osteopor s and osteosclerosis.

► [Undoubtedly the authors are interested in receiving additional reports of -ray findings of bones in urticaria pigmentosa. The idea of central registry for the more uncommon dermatoses and syndromes associated with cutaneous lesions is an excellent one —Eds.]

Bone Changes in Kaposi's Sarcoma Analysis of 15 Cases Occurring in Bantu Africans. In idiopathic multiple hemor rhagic sarcoma, the card nal change consists of new capil lary formation in the dermi ma nly made up of blood es sels with a few lymph vessels and connective tissue hyper plasia Hemorrhages may be seen Although Kaposi s sar coma is primarily a skin disease, lesi ns have been found in nearly every organ. A G M Davies[3] (Kampala, Uganda) describes bony changes seen n 15 Bantu Africans with Ka posi s sarcoma. The hanges were much more frequent in bones of the feet than of the hands. The tibiae and fibulae were the other limb bones most frequently affected.

Un form usually severe rarefaction was f und i the feet of 10 patients, but not in the hands. It was present in 6 of 33 lower limb long bones examined. In cases with this change the medullary cavity was expanded and the cortex thinned from with n.

Localized eas of ntense rarefaction had ll defined and usually irregular margins. The trabeculae were scanty and appeared partially erased. They were most common in the spongiosa of the bases and heads of the toes but wer also found n the tarsals and metatarsals and the bones of the fingers Occa sionally uch areas appeared to have broken through the bone cortex

Cystl ke areas were round or oval with clearcut borders, arying from 2 to 10 mm. n diameter They had the same dis-

3) J Fac. Radiologists 8 32-40, July 1956

tribution as localized areas of intense rarefaction but in only one patient had they broken through the bone cortex. Usually they seemed to accommodate themselves to the normal bony outline and were even squashed together becoming polyhedral. They never involved the joints. Some cysts had clear centers whereas others were traversed by a few coarse trabeculae. They showed no cyst wall and produced no surrounding bone or periosteal reaction. The clear cystlike spaces might closely resemble radiologically the pseudocysts of the extremities in sarcoidosis and had similar distribution.

Superficial cortical erosions were present in one or more bones of 10 patients. It was commonest in the phalanges and metatarsals of the feet. The appearance of the eroded surface varied considerably. Complete destruction of bone was seen in only one patient. It involved a metatarsal bone and resembled the changes in purely osteolytic bone sarcoma. Calcification of a metatarsal artery was encountered once. Biopsy specimens from the bone lesions were not obtained.

Differential diagnosis is from multiple myelomas and osteolytic metastases, gout, multiple chondromas, sarcoidosis and Madura foot.

► [As is pointed out by Davies in the original article, bone changes in Kaposi sarcoma repeatedly have been mentioned in the literature. In addition to the diseases listed by the author, urticaria pigmentosa is another differential diagnostic possibility when such bone changes are found. —Eds.]

Gunther's Sebocystomatosis. Marco Dogliotti and Mario Visetti[4] (Univ. of Turin) discuss two cases from the genetic standpoint.

CASE 1.—Woman, 38, asthenic, in fair general condition, with slight protrusion of characteristic shiny eyeballs associated with tremor of the fingers, had numerous nodules on the flexor surface of the forearms (Fig. 37), on the chest and the back and, in smaller number, on the medial surface of the thighs and on the breasts. The cysts, which varied from pinhead to large pea size, were either isolated, in groups or arranged in large number in a line that followed the major axis of the arms. Histologic study showed cysts in the deep derma and hyperplasia of the sebaceous glands. The first nodules had appeared when the patient was 11, at the time of menarche. Menstruation had always been irregular in rhythm and duration, but regular in quality and quantity. The father was in good

(4) Minerva dermat. 31:210-215, July 1956.

health, but the mother had cysts bilaterally in the axillary region and sebocystomatosis had been diagnosed in the past.

CASE 2.—Man, 25, in good general condition with no organic impairment, had small nodules on the chest and flexor surface of the arms for two years. Histologic findings were similar to those in Case 1 except that the sebaceous glands were normal. There was no history of dermatologic conditions in any member of the family.

Findings in Case 1 seem to support the theory that Gunther's sebocystomatosis is a familial condition linked to endo-



FIG. 37.—Numerous nodules localized on flexor surface of arms. (Courtesy of [illegible], M. and [illegible], M.: Minerva dermat. 31:210-215, July 1 [illegible])

crine disturbances (in this case dysmenorrhea and dysthyroidism). Since this genetic theory does not apply to Case 2, the authors feel that Gunther's sebocystomatosis should be considered a condition arising from cysts that form on a dysplastic base rather than from retention cysts. Like other genodermatoses, it may develop at any time in a person's life, conditioned or not by other factors. The disease, not necessarily congenital, should be classified among nevoid conditions.

► [This dermatosis is perhaps better known as steatocystoma multiplex. In addition to these lesions, other developmental abnormalities may be present, e.g., faulty dentition.—Eds.]

Cutaneous Manifestations of Multiple Myeloma were studied by Samuel M Bluefarb[3] (Northwestern Univ) The disease occurring mostly in persons aged 40-70 is characterized by focal or diffuse abnormal overgrowth of plasma cells. Plasma cells are sharply defined and have heavy chromatin aggregations in the nucleus, basophilic cytoplasm a clear space in the nucleus and an eccentric nucleus. Nondermatologic features of the disease are pain in the bones pathologic fracture neurologic and gastrointestinal symptoms fever splenohepatomegaly extramedullary lesions roentgen abnormalities and pulmonary involvement Roentgen changes of the skull are typical with rounded punched-out, sharply marginated areas and no surrounding osteoblastic reaction. Important hematologic findings are anemia, excess rouleau formation immature red and white cells atypical plasma and myeloma cells lymphocytosis and eosinophilia, and elevated sedimentation rate Bence Jones proteinuria and hypercalcemia with normal alkaline phosphatase are also present.

Specific cutaneous manifestations are extramedullary plasmacytomas of the skin and mucous membranes and skin tumors following extension from the bone. Nonspecific cutaneous manifestations are due to the following underlying conditions (1) abnormal proteins as in amyloidosis cryoglobulinemia and hyperglobulinemia (2) cytopenias such as anemia, associated with glossitis pallor and koilonychia, leukopenia with pyodermas and agranulocytic membrane and thrombocytopenia with tendency to hemorrhage (3) toxic lesions such as erythemas and pigmentations, alopecia, icthyosiform atrophy of the skin and seborrhea like dermatitis, and (4) myelomatous involvement of internal organs such as the kidney with pruritus pitting edema and uremic frost the lungs with disappearance of lunules from the nails and clubbing of the fingers and nerves and ganglions with herpes zoster due to pressure on the ganglions from extension of bone tumor

Current treatment measures for multiple myeloma are

(3) A.M.A Arch. Dermat. 72 506-522, December 1955.

(1) excision of solitary lesions (2) roentgen therapy of involved bones (3) stilbamidine for symptomatic pain relief (4) urethan, which appears more effective in chronic cases (5) corticotropin and cortisone, which seem to produce clinical remissions, and (6) combined therapy with steroids and urethan, which seem to act synergistically seems most promising at present.

Clarification of the position of the plasma cell studies of the abnormal proteins and improvement in treatment are needed.

Pathogenesis of Erythrodermas in Chronic Lymphatic Leukemia. Two pertinent cases are reported by J J Herzberg[4] (Un of Hamburg)

CASE 1.—Woman, 48, with redness, scaling and swelling of the feet two years previously and subsequent cutaneous changes over



Fig 38.—Left forearm, showing millet-seed-sized, red nodules, some in sharply outlined infiltrated plaques, with purpuric macules above nodules. (Courtesy of Herzberg, J J Arch klin exper Dermat 202 208 223 1956.)

the entire body on hospitalization showed general redness, swelling and branny scaling, with numerous, millet-seed-sized, red nodules, which occasionally formed larger plaques, on top of which there were purpuric macules (Fig 38) Between the lesions, brighter nonatrophic areas were present Intertriginous oozing crust formation and large hemorrhagic blisters were seen. There was intense itching, gradual loss of hair koilonychia and some opaqueness and brittleness of the nails. Sweat and sebum were reduced. There was general

(4) Arch klin exper Dermat 202 208 223, 1956.

adenopathy with partly confluent, enlarged, soft lymph nodes. The pulmonary hilus showed densities the spleen and liver were enlarged. Normal granulocytopoiesis and atypical cells were found in the bone marrow The white blood cell count was 164,000-360,000. Histologic study revealed edema of the skin and infiltration by masses of lymphoid cells, histiocytes, proliferating reticulum cells, a few lymphoblasts neutrophils plasma cells and some monstrous cells with large nuclei Mitoses were numerous and partly pathologic. There were moderate networks of argyrophilic fibrils.

CASE 2.—Woman 54 with dry slightly pruritic redness of the skin of sudden onset and coarse lamellous exfoliation six months later on hospitalization showed generalized redness. The skin was extremely dry and exfoliating Large hemorrhagic blisters and marked cutaneous atrophy were present on the acra. There were general lymphadenopathy and spleno- and hepatomegaly The bone marrow was rich in cells and displayed numerous lymphatic elements, Gumprecht s shadows and intensely proliferating erythro- and granulocytopoiesis. The white blood cell count was 22,100-71,000. Rapid loss of hair and baldness occurred, with exfoliative changes. The nails were characterized by koilonychia, onychogryposis and opaqueness. Sweat and sebum were reduced. Histologic study showed edema and vacuolation of the basal cell layer maximal edema of the skin and infiltration by lymphoid cells and a few histiocytes. No argyrophilic fibrils were seen.

The first case is definitely one of lymphadenosis cutis universalis in which the pathogenesis of cutaneous manifestations can be explained satisfactorily by organoid lymphatic metaplasia of the skin Explanation of the pathogenesis in the second case is more difficult. Neither a nonspecific nor a leukemid reaction can be assumed the latter because of the wide extent of the disease cutaneous atrophy total loss of hair with baldness and shedding of nails. Such types of general involvement cannot be explained satisfactorily at present Erythrodermas with tumor formation and the appearance of specific infiltration should be considered as transitional to lymphadenosis cutis universalis. Similar erythrodermic variants exist in the group of reticuloses, particularly mycosis fungoides For nonspecific erythrodermas and also the nonspecific complication of pruritus a central dysfunction is probably of pathogenic significance.

Evaluation of Cutaneous Smears in Lymphoblastomas of Skin is presented by Kaare Getz Gertrude L. Pease and Hamilton Montgomery[7] (Mayo Clinic and Found) Touch smears and imprints were made from specimens of skin re-

(7) A.M.A. Arch. Dermat. 74 86-91 July 1956

moved for biopsy in 19 patients with lymphoblastomas. Evidence of a neoplastic process was revealed in seven the histopathologic and cytologic find ngs in some of these are illustrated in Figure 39

The cutaneous smears were of special value in confirming diagnosis of cutaneous lymphoblastomas and sometimes in classification of the type of lymphoblastoma. The presence of

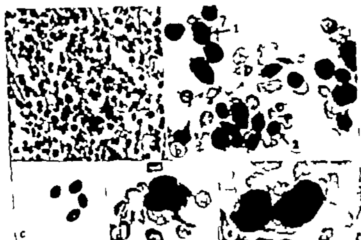


Fig. 39.—a (reticulum cell sarcoma—smears of peripheral blood negative) section reveals dense infiltrate; many cells are irregular in size, with hyperchromatic nuclei and nucleoli, and resemble reticulum cells. Hematoxylin-eosin; reduced from [illegible]. b (same case) touch smear reveals large immature cells of reticulum type as in contrast to normal lymphocyte at 2. Wright's stain; reduced from 1000. (case of mycosis fungoides, tumor stage—smears of peripheral blood negative), touch smear reveals nest of immature mononuclear cells. Wright's stain; reduced from [illegible] d and [illegible] (same case) large binucleated cells strongly suggestive of Reed-Sternberg cells. Wright's stain; reduced from 1000. (Courtesy of Goss, L., et al.: A.M.A. Arch. Dermat. 7 [illegible], July 1956.)

cells of varying degrees of immaturity in most instances of my on fu goides that were studied is additional evidence that this condition belongs in the group of lymphoblastomas.

In a study of a control series of cutaneous smears in 59 cases f benign dermatoses a fair number disclosed an occa ional immature cell. These cells, however were not so nu merous nor so immature as those found n proved cases of lymphoblastoma. Thus, the occasional appearance of imma ture white blood cells in a cutaneous smear is not enough to warrant posit e diagnosis of lymphoblastoma.

Cutaneous touch and imprint smears are readily made at the time the specimen is taken for biopsy and these smears, quickly and easily prepared can be studied later after suitable staining

Acquired Ichthyotic Syndromes, according to Julio M. Borda Sergio G Stringa Jorge Abulafia and Manuel Villa[1] (Buenos Aires) may be caused by vitamin A deficiency hypothyroidism and diseases of the reticular system (Hodgkin s disease lymphosarcoma, reticulosarcoma mycosis fungoides polycythemia vera) Nutritional deficiency resulting in ichthyosis may be due to poor diet, digestive disorders, such as chronic diarrhea, chronic alcoholism etc. or to wasting from severe dieting or visceral neoplasms

Man 61 on restricted diet for seven months because of gastro-intestinal symptoms attributed to duodenal ulcer for past two months showed deterioration of the general condition, with severe weight loss and cutaneous manifestations indistinguishable from true ichthyosis. Blood level of vitamin A was 11 μg./100 ml. (36.34 units/100 ml) and carotene could not be measured. He died a month after examination autopsy revealed a gastric adenocarcinoma with metastases in the liver and pancreas.

In hypothyroidism ichthyotic lesions may accompany the usual skin changes (pale skin xanthosis mucous and cutaneous myxedema hyperpigmentation etc.) Ichthyosis probably results from decreased thyroid function through interference with normal metabolism of carotene A woman, aged 74 with hypothyroidism showed ichthyosi other cutaneous symptoms macroglossia hoarseness and general manifestations including mental dulness anemia and high blood cholesterol levels Serum carotene level was 2.6 units. Treatment with 0 10 Gm thyroxin daily for two months improved the general condition and the skin lesions decreased

In some cases of reticuloendothelial disease keratotic ichthyosis may precede other clinical signs and have diagnostic value. Vitamin A index, response to vitamin therapy and other findings suggest that ichthyotic lesions are partly due to disturbed vitamin A metabolism Ichthyosis based on reticuloendothelial disea e was observed in three patients with Hodgkin s disease (one a boy aged 8, and one with mycosis fungoides)

(1) Arch. argent. dermat. 6:47-61 March, 1956.

A woman, aged 4.., with clinical Hodgkin's disease for 2½ years, showed a cutaneous ichthyotic condition coinciding with a relapse. Serum vitamin A level was 8.77 µg/100 ml. (28.94 unit) carotene 10.96 µg/100 ml. Vitamin A therapy (100,000 units) with cortisone and nitrogen mustard resulted in notable clinical remission and almost complete disappearance of skin lesions. Serum vitamin A had increased to 17.55 µg./100 ml about double the previous level serum carotene le el had remained the same.

Ichthyosiform Atrophy of Skin in Hodgkin's Disease was observed by Francesco Ronchese and Donald C. Gates.

Man, 50, presented definite ichthyotic features in consistence and pathology of the skin. A peculiar dryness became more apparent with increase in severity of the symptoms of the disease, but it disappeared and the skin returned to apparent normalcy repeatedly on treatment with x-ray and nitrogen mustard. The skin changes affected the entire body including the flexures and creases.

This is the 11th case reported. Even if such a manifestation i apparently nonspecific, Hodgkin's disease or some other lymphomatous disease should be considered when a sudden change of kin texture from normal to ichthyos form occurs.

Poikiloderma Atrophicans Vascularis in Malignant Lymphogranulomatosis Paltauf-Sternberg is reported by Helm t Tritsch and Werner Kiessling[1] (Uni of Heidelberg)

Man, 50, had had rough and dry skin since age 23 and asthma since 1940, for which he had taken si to eight doses daily of antimony sulfate-containing drug from 1951 to 1954 Since November 1952 he had had redness and scaliness of all the skin, with no pruritus. On hospitalization (March 2, 1953) the entire integument was dry bluish red to melanotic, and showed numerous flat, bluish red, small papules The oral mucosa was free from lesions. There was loss of hair on scalp, in the axillae and the pubic region. The nails were hard and brittle. I the axillae, groins and right retroauricular region, indolent, mobile lymphadenopathy existed. Antimony poisoning as excluded by laboratory examination of urine, blood, skin, hair and nails. Skin biopsy revealed poikiloderma atrophicans vascularis and ichthyosis. In 1954 tumor formation developed, with subsequent ulceration on the left cheek, nose and left leg

On hospitalization, he wa cachectic, the skin was dry rough and of variegated appearance showing a fine reticular network of bluish brown areas, normal or depigmented islands and fine telangiectasia. Atrophy and paper-like condition were particularly marked on the trunk scaliness was scarcely noticeable. Irregular loss of scalp hair and more pronounced brittleness of nails were present. The left

(¹) New England J. Med. 255 ... Aug. 9, 1956
( ) Arch. klin. u. exper. Dermat. 202 ... 1955.

half of the face showed marked swelling with serpiginous ulcerations, the left eye was occluded by an egg sized firm tumor. Multiple lymphadenopathies were seen. Melanin was present in urine and excretion of 17 ketosteroids was reduced (11.5 mg./24 hours). Increased asthma, rise in temperature to 100-102 F, diarrhea and loss of weight occurred. Three weeks before death, a punch biopsy from one of the facial ulcers revealed lymphogranulomatous changes. Autopsy showed lymphogranulomatosis of lymph glands of neck, hilus pulmonis, hepatic portal vein, parapancreatic and para-aortic lymph nodes and nodular, partly ulcerated, partly cicatrized lymphogranulomatosis of the facial skin and small lymphogranulomatous nodules in the lungs, particularly subpleural. Fat depletion of the adrenal cortex and fresh spotty necrosis of the zona fasciculata were also seen. The inguinal glands showed nonspecific inflammation and minor melanin deposits.

Poikiloderma atrophicans vascularis is not a morbid entity but rather a condition of the skin that follows various dermatoses, particularly granulomatous processes. It also has been seen preceding mycosis fungoides. In 53% of cases, cutaneous changes were only partly specific, being mostly nonspecific, e.g., erythrodermatic, ichthyosiform.

In the authors' case the onset with epidermal hyperplasia is remarkable, as is increased formation of melanin deposits which were possibly due to the adrenocortical changes ascertained at autopsy. Hemosiderin deposits rarely described in the condition may be explained by diapedesis of red cells from dilated blood vessels. Tumor allergic processes may be assumed in the pathogenesis of erythroderma and poikiloderma. Lymphogranulomatosis was believed to be due to a disease of the nuclear apparatus with giant cells resulting from abnormally stimulated formation of protein bodies. Since the latter are probably faulty (heterologous proteins) defense mechanisms are stimulated, which in predisposed persons may lead to nonspecific cutaneous lesions.

► [The ichthyosis-like changes which had been present for 27 years may well have been the first evidence of Hodgkin's disease in this patient. If this is the case, it would indicate the relatively benign course of the disease, without treatment, over the years.—Ed.]

Scabies Norvegica and Lymphatic Leukemia. Scabies norvegica has been described in patients with low hygienic standards and such chronic debilitating disturbances as diabetes, avitaminosis and malnutrition. A. Dostrovsky, F. Raubitschek and F. Sagher[2] (Hadassah Univ. Hosp., Jerusalem) observed a woman, 55, with scabies norvegica and

(2) Dermatologica 113:26-34, Jul., 1956.

emaciation due to leukemia. Invasion of the skin by the Sarcoptes was greatly enhanced. Erythroderma is known to occur both in leukemia and in norvegian scabies. In this patient it cleared after energetic antiscabies treatment only then did the original leukemic infiltrations become apparent. At about the same time, a herpes zoster-like leukemic skin eruption appeared. It seemed, therefore, that the exfoliative dermatitis was mainly caused by the scabies norvegica. The severe general state caused by the leukemia, and the lack of large hyperkeratotic masses in this patient explain the purely accidental detection of the parasitic disease.

A hospital epidemic occurred among 25 contacts, but no mites could be detected by direct search or in serial sections of two biopsy specimens. The rapid spread of infection in this epidemic seemed to be due to the vast masses of parasites contained in the scales shed by the patient. Judging from the regular type of scabies seen in two members of the patient's family it is assumed that the parasite causing scabies norvegica in this patient was the common type of Sarcoptes scabiei var hominis.

The contact patients showed an atypical clinical picture similar to that in scabies contracted from animals.

► [Perhaps the simultaneous occurrence of scabies norvegica and leukemia is based on the same mechanism as the reported coincidence of superficial or deep fungous infections and various forms of lymphomas (see for example Cawley and Curtis (J Invest. Dermat. 11 443, 1948) and Lewis, Hopper and Scott (A.M.A. Arch. Dermat. & Syph. 67 247 1953) —Eds.]

Exfoliative Dermatitis Associated with Carcinoma of Lung was observed by B McGaw and V J McGovern[3] (Royal Prince Alfred Hosp Sydney) in three men, in whom the dermatitis was present before symptoms of the carcinoma became manifest.

CASE 1—Man, 49 was hospitalized with psoriasis and occasional cough. The rash became more disseminated and of the nature of exfoliative dermatitis. Skin biopsy showed nonspecific dermatitis. Autopsy revealed exfoliative dermatitis and carcinoma of the left upper lobe bronchus, with widespread metastases.

CASE 2—Man, 63, first showed rash on both legs, gradually spreading upward. On penicillin, the rash became worse and soon covered the whole body with erythema and scaling. There was marked pruritus. Later the face and legs became edematous and a blue-gray pigmentation of the skin appeared. He had slight cough and enlarged glands in both groins and axillae. Skin biopsy showed

(3) Australian J. Dermat. 2:113 ID June, 1954.

chronic nonspecific inflammation, and lymph node biopsy dermatopathic lymphadenopathy The cough produced thick viscid sputum. Autopsy revealed an anaplastic carcinoma of the left lower lobe.

CASE 3—Man 57 had had a generalized itchy rash which was red *and scaling for six months.* X rays revealed a rounded opacity at the base of the right lung Examination showed generalized erythema with occasional areas of scaling The keratin layers of the palms and soles were thickened, and there was thick crusting throughout the scalp Numerous small verrucous vegetations were present on the trunk. The right lung was removed because of a lower lobe squamous *cell* carcinoma. Three weeks after surgery the rash and verrucous vegetations started to clear

Steroid hormone therapy caused little or no improvement in the skin condition of any of these patients

► [This presentation again calls attention to dermatoses which should make one suspicious of and examine for internal malignancy e g dermatomyositis, acanthosis nigricans, herpes zoster etc. The possibility of purely *coincidental* occurrence of malignant internal disease and a given cutaneous disease cannot be excluded, unless the coincidence is found in an adequate number of cases in a sufficiently large sample of patients or unless there is a significant frequent simultaneous occurrence of the two diseases in a smaller series. The editors are not aware that malignant tumors of *the lungs* have been *found even in a very small fraction* of the many thousands of cases of exfoliative dermatitis which have been seen by dermatologists and some of which must have come to autopsy Further studies in this important area are indicated in view of the report of McGaw and McGovern.—Eds.]

Primary Skin Cancer of Fingers Simulating Chronic Infection was observed by H T John[4] (Univ College Hosp. Med School London) Primary skin cancer of the fingers is usually a squamous cell carcinoma or a malignant melanoma, and actually three of the author s cases proved to be squamous cell carcinoma and two malignant melanomas. Basal cell carcinoma is relatively rare Squamous cell carcinoma may arise in an area previously irritated chemically mechanically by irradiation or in a benign tumor It often takes the form of a mass of exuberant granulations, slowly enlarging and involving the surrounding skin and covered with a seropurulent or sanguineous secretion which rapidly becomes malodorous from necrosis or infection with saprophytic organisms The granulations bleed easily and hemorrhage may be brisk Pain is sometimes severe. Melanoma of the fingers may arise in a long standing mole but the subungual tumor commonly arises from an apparently normal nail bed

(4) Lancet 1 642 644 May 12, 1956

It is suggested that biopsy should be done if a chronic lesion of a finger persists despite treatment and in the absence of an adequate local or general cause such as a reta ned dead nail or foreign body osteitis or vascular disease Any apparent chronic granulomatous les on with bluish pigmen tation must be initially viewed with suspicion. Benign le sions of the nail bed, such as subungual fibroma, subungual exostosis or glomus tumor neither break through the nail nor invade the skin. Malignant lesions at this site however lift the skin and nail and eventually replace them with fungating tumor

Malignant Change in Erythema Ab Igne is reported in four patients by G A. Grant Peterkin[8] (Royal Infirm Edin burgh) All were women aged 71 80 56 and 57 All lesions were on the legs and thighs and were ulcerating hyper trophic and verrucous n appearance. All patients had his tories of prolonged intermittent exposures to heat in the areas involved. Histologic examination of biopsies of the involved areas revealed the chronic inflammatory changes of erythema ab igne with parakeratosis, edema, cellular infiltra tion and formation of vascula granulation tissue in some areas and changes of squamous cell epithelioma in others. In a fifth patient squamous cell carcinoma was suspected, but the lesion proved to be a premalignant keratosis. Two of the four patients with carcinoma had been cured of cancer in other organs previously and the other two had skin changes diagnosed as poikiloderma atrophicans vasculare a d sease which may be the first sign of an internal malignancy

Th disease, beginning as acute erythema after exposure to heat of a coal fire, subsided and then recurred after subsequent exposures. Retiform pigmentation appeared on the skin over the deep veins. Subsequently hyperkeratoses appeared, which gradually changed to squamous ell carcinoma In general, the malignancies are of low grade with no evidence of secondary spread and with a good prognosis. With imilar exposures to coal fires, no males hav shown these changes. It is suggested that endocrine factors play an unknown part in prod ction of the lesions.

Squamous Epithelioma Possibly Induced by Therapeutic Application of Tar Unlik occupational tar cancer carcino-

(8) Brit. M. J. 2:1599 1955, Dec. 31, 1955.

ma induced by therapeutic application of tar is extremely rare. Besides the following case presented by A. J Rook, G A Gresham and R. A Davis[6] (Cambridge Univ) only four cases have been reported in which therapeutic application of tar may have induced malignant change. In three patients coal tar had been applied for 3 months, 6½ years and 8 years in one pine tar had been used for 23 years. All patients were men

Man 60 was a roadworker for 25 years. He was occasionally present at tar laying operations, but neither he nor his clothes were contaminated with tar At age 26 he noticed an irritable eruption in the groins which persisted ever since and which later extended to the pubes and inner thighs. Apart from a brief period 2 years after onset, he did not consult a doctor for 27 years, but treated himself with various ointments, many containing tar Six years before hospitalization, a paste was prescribed for him containing prepared coal tar 3% he applied this for five years. For 18 months before admission he used a proprietary ointment containing 2.2% oil of cade. During the 34 years he used at least 1 oz. of ointment or paste every fortnight. About a year before hospitalization, a "spot" appeared on the front of the left thigh. It enlarged steadily ulcerated and was occasionally painful He had not received x ray therapy to the area nor was there a history of arsenic intake.

On examination, the skin of the pubes, inguinal flexures and upper and inner thighs was grossly lichenified patches of hyperpigmentation and leukoderma dappled the rough and thickened area. On the lichenified skin of the upper left thigh were two indurated foul-smelling fungating ulcers the upper measured 2×2 cm. and the lower 5×4 cm. There were small shotty lymph nodes in the left groin. General physical examination showed no abnormality

Skin surrounding the tumors was widely excised with a block dissection of the left inguinal nodes. A Thiersch graft from the right thigh was sewn over the raw area and healed soundly Histologic examination showed a well differentiated keratinizing squamous cell carcinoma penetrating the underlying corium.

The great rarity of medicinal tar cancer may be due to the relative inactivity of the carcinogenic factors when tar is incorporated in paste and ointment bases. Prolonged application of tar in aqueous or alcoholic solution or in water miscible bases may involve greater carcinogenic risk

► [We are in complete accord with the authors when they state that the epithelioma in this case *may possibly* have been induced by the applications of tar After 34 years of chronic dermatitis it is indeed doubtful whether the tar can be blamed for the malignant proliferative changes.

Irrespective of whether tar was the cause of malignant changes in this particular case, the extreme infrequency of such reports attests to the rela-

(6) Brit. J Cancer 10 17-23 1956.

the safety of tar as used in topical dermatologic therapy. When one considers the millions of therapeutic tar applications on human skin which are undoubtedly made each year including patients who use tar preparations for prolonged periods, it is encouraging to realize that where skin cancer is found in such treated areas, the etiologic role of the tar still remains very much in doubt.—Eds.]

Mortality Rate from Skin Cancer at the University of California Visible Tumor Clinic, from 1935 through 1954 was 1.65% or 35 of 2,122 cases of basal and squamous cell carcinoma of the glabrous skin. Basal cell epitheliomas were most common in the orbital auricular and malar areas squamous cell epitheliomas, in the auricular and nasal regions and dorsum of the hand. Metastasis did not occur in any of the 11 patients with basal cell epithelioma but did in 15 of the 24 with squamous cell carcinoma. Edward A. Levin[7] analyzed the 35 deaths, but found no constant factors or circumstances other than "too little or too late treatment. In a few death occurred despite apparently adequate treatment and lesions in these cases were considered radiation resistant.

Skin cancer should theoretically approach a 100% cure rate with two simple rules (1) early medical advice should be sought for all suspicious growths moles or warts and (2) after exact diagnosis by biopsy the first treatment given, whether surgical, chemosurgical, electrosurgical or x ray should be complete and adequate for the first time yields the best opportunity for cure.

► [It would be interesting to know the actual causes of death in these 11 patients with basal cell epithelioma which did not metastasize.—Eds.]

Rodent Ulcers in Identical Twins are reported by A. G. Oettle[8] (Johannesburg) The occurrence of similar simultaneous and symmetrical tumors in monozygotic twins is always noteworthy the following example of true basal cell epithelioma in twins appears unique. Unfortunately histologic confirmation was lacking in one.

Male twins, 36, were regarded as identical twins on the basis of blood groups, appearance, susceptibility to disease and fingerprints. One had cystic rodent ulcer over the right mastoid area on which no biopsy was performed as the lesion was regarded as a typical basal cell epithelioma. It became necrotic on x-ray therapy and disappeared, leaving a flat papule the color of the surrounding skin about 1/8 in. in diameter which was excised. Histologic examination showed calcinosis circumscripta but no evidence of ulceration or neoplasm.

(7) California Med. 83 443-445, December 1955.
(8) A.M.A. Arch. Dermat. 5 370-372, August, 1956.

The twin had a similar lesion in the same area about two years later which, however had ulcerated and was somewhat crusted. The size was similar and the edges were translucent and pearly around the papule. It was excised and examined histologically revealing a typical basal cell epithelioma, and in one place it completely invested an adult hair no trace of the follicle remaining. The tumor had penetrated to the deepest layer of the dermis adjacent to the superficial hypodermic fat.

The eldest brother of these twins had a rodent ulcer on the forehead at age 36 years. Apparently there is a hereditary susceptibility for rodent ulcers in this family.

► [The genetically determined predisposition to disease is made particularly evident in these twins. In addition to the basal cell epitheliomas, they had appendectomies within two years of each other and both had tinea pedis of the left foot at the same time although they were geographically separated!—Eds.]

Erythroplasia of Queyrat. Evaluation of Nature of Condition Based on Critical Review of World Literature and Analysis and Tabulation of All Published American Cases and Material Collected from 1933 to 1954 at Skin and Cancer Unit of New York University Hospital. Saul Blau and Arthur B. Hyman[9] maintain that true erythroplasia of Queyrat is Bowen's disease, a malignant condition modified clinically by its location on mucous membrane. From the literature, it is concluded that erythroplastic lesions of the penis cannot be differentiated clinically as benign or malignant, but histologically can be defined as (1) Bowen's disease of the mucous membrane, (2) benign inflammatory dermatoses of the mucous membrane or (3) plasmocytoma penis.

The commonest site of an erythroplastic process is the glans penis. The smooth, red plaque is usually solitary and has a moist, glistening, lacquered appearance described as "red velvet." The lesion is round, oval or irregularly lobulated and is sharply differentiated from the surrounding tissue. It is level or slightly raised and the surface is granular or mammillated. There is no tenderness or pain, but the patient may complain of a mild itch. Adenopathy is absent and no significantly associated systemic diseases have been observed. Because of chronicity and indolence, the plaques may be seen with leukoplakia, verrucous keratoses and vegetations. The histologic appearance corresponds to that of Bowen's disease or of plasmocytoma penis. Typical bowenoid features are variety of cell and nuclear size, shape and staining

(9) Acta dermat.-venereol. 35: 341-378, 1955.

quality cellular monstrosities multinucleate cells increased mitoses intracellular edema and dyskeratotic forms of the grains and corps rond types. In the inflammatory or plasmocytic types there is usually a crust and parakeratotic scale, thin suprapapillary plates, proliferating rete pegs and either an inflammatory infiltrate or a heavy plasma cell infiltrate In some there may be more edema and spongiosis, but the basal margin is usually sharp and intact

Analysis of 62 American cases of clinical erythroplasia showed definite histologic signs of malignancy in 16. Erythroplasia of Queyrat is like carcinoma of th penis in that it occurs only in the uncircumcised. In 26 cases there was no histologi evidence of malignancy these were diagnosed plasmocytoma penis or one of the benign inflammatory states. A mixed group of 20 cases was excluded on clinical grounds.

Bowen disease of mucous membran can properly bear the eponym of erythroplasia of Queyrat, but nonmalignant inflammatory appearances should not have the title. Plasma cell infiltrates n mucosal sites may be an ent ty beari g the title plasmocytoma penis. Circumcision at birth practically precludes the possibil ty of any subsequent lesion of the glan penis being maligna t.

► [See also the article, Puzzling Persistent Penile Plaques, this YEAR BOOK, p 241 —Eds]

Premalignant Fibroepithelial Tumors (Pinkus) H Jaeger a d J Delacrétaz (Uni of Lausanne) report two cases.

CASE 1 —Woman, 76, had skin tumors on the back, mainly in the lumbar area for some years. On examination, about a dozen lesions ere seen in the lumbar region, some of which resembled seborrheic warts and pagetoid epitheliomas but most were pinhead- to pea-sized, slightly projecting, firm, smooth-surfaced, rose-colored tumors (Fig 40) Histologic study (tumors, *1 4 5 7 8*) revealed characteristic changes of premalignant fibroepithelial tumor consisting of epithelial and fibromatous proliferation. The former displayed a fine network of epithelial strands with arying enlargements here and there and the typical histologic appearance of basal cell epithelioma, just as the small buds which form along the epithelial strands F bromatous hyperplasia involving the connective tissue of the papillary layer and upper corium formed round masses hich stretched the epithelial strands, similar to intracanalicular fibroadenoma of the breast. Tumor 3 and 6 showed similar changes and tumor 9 those of a typical seborrheic wart tumor *10* was classic basal cell epithelioma.

( ) Dermatologica 112 344-370 Apr June, 1956.

CASE 2.—Woman 83 had two lesions for four to five years, one on the right lower eyelid showing a crusted center and pearly border the other in the right popliteal fossa, was an elliptic, multilobulated, firm, mobile, painless tumor 15×30 mm, covered by crusty-scaly masses and ulcerated at its poles. There were no adenopathies. The first tumor was a basal cell epithelioma the second corresponded histologically to tumor *1* of Case 1

Premalignant fibroepithelial tumors described first by



FIG 40—Tumors *1-8* fibroepithelial; *9* verruca seborrhoica; *10*, multicentric basal cell epithelioma (Courtesy of Jaeger H., and Delacretaz, J Dermatologica 112 364-370, Apr June, 1956.)

Pinkus are rare Degos and Hewitt presented two additional cases The authors two cases are remarkable in that the second exhibited a localization not hitherto described the first displayed (like cases 1 and 4 of Pinkus and 2 of Degos and Hewitt) the association with seborrheic warts finally because both showed also basal cell epitheliomas (as in cases 1 and 4 of Pinkus and case 1 of Degos and Hewitt) Premalignant fibroepithelial tumors belong to the group of basal cell epitheliomas

Multiple Growth of Molluscum Sebaceum in Donor and Recipient Sites of Skin Graft is reported by F A Dibden and Malcolm Fowler[2] following removal of two "squamous cell carcinomas of the back of the hand

Man, 76 had two red nodules that had grown in two months on

(2) Australian & New Zealand J Surg 25 157 159 November 1955.

the right hand. These lesions were excised and a split graft, 5×8 cm., as applied to the area of the dorsum of the hand. Two months later he *returned with three lumps on the donor site on the* right thigh and three on the recipient site on the right hand (Fig 41) The lesions were raised, rounded, smooth nodules, tomato red with central horny plug suggestive of *molluscum sebaceum*. Histologic sections from the edge of the hand nodules showed thick, folding squamous epithelium, well differentiated, with some keratinous plugs on the surface. In none of the sections was there any *nuclear pleomorphism* or abnormal mitotic activity Diagnosis of molluscum



F —Large lesion on radial edge of graft, with two smaller lesions on proximal and ulnar borders. (Courtesy of Dobson, F. A and Fowler M Australian & New Zealand J Surg 25 57 159, November 955)

sebaceum was made. The lesions of the thigh disappeared in two months without treatment and those of the hand in three months, except for one side of the largest lesion. This and one new lesion at the periphery of the graft involuted slowly after small doses of x-ray therapy

The multiple character of the lesions nd the appearance a distant donor graft site suggest an infecti e process. The circumstances may also indicate a traumati basis with seq estration of epith li m followed by proliferation. Thus it important to mak correct diagnosis to avoid the appar ent risk of inflicting further lesions by unnecessary surgical ction Curetting the lesion t the keratotic stage is adequat for microscopy and will ind cate absence of infiltration.

► [The importance of establishing the diagnosis of tumors of the skin before instituting therapy and to avoid unnecessarily extensive forms of therapy cannot be stressed enough Unfortunately those trained in major surgery usually have not been trained in the basic principles of dermatologic differential diagnosis they lack the ability of the ell-trained dermatolo-

gist to recognize clinically and differentiate between the many types of skin lesions as well as his knowledge of the many different therapeutic modalities which may be used in the management of the various lesions—Eds.]

Molluscum Sebaceum, sometimes termed keratoacanthoma is discussed by C D Calnan and H Haber[1] (St John's Hosp for Diseases of Skin London) The multiple familial self healing epithelioma of Ferguson Smith may be similar but there is usually a family history and the lesions



Fig 42 Early stage in spontaneous involution. (Courtesy of Calnan, C. D and Haber H J Path & Bact. 69 61-66, Jan. Apr 1955.)

are numerous The tumor like keratosis of Poth is closely related follows sunburn and appears on the back of the hands and forearms

The age incidence of molluscum sebaceum in the authors patients was 15 78 but most were 40-70 Clinically rapid growth to maximal size in four to eight weeks is followed by slow involution in two to four months if left untreated. Rarely is more than one lesion present ulceration is unusual The fully developed tumor (Fig 42) is about 1 cm. in diameter dome shaped with a central horny plug or crust. The convex sides are smooth not translucent like basal cell epithelioma and fine telangiectatic vessels can be seen on

(1) J Path. & Bact. 69:61-66, Jan. Apr 1955.

the surface. There may be an antecedent history of mild trauma. Gas, tar and oil workers sometimes have recurrent lesions of this type. Spontaneous involution has been observed and is accepted by dermatologists in England. The common forms of treatment are cur ttage with galvanocauterization of the base simple local excision or radiotherapy in the amount of 1,500 r at 90 kv

Histologically the lesion starts with hyperplasia of a group of foll cles, leading to hyperkeratosis and acanthosis with irregular downgrowth to the sweat gland le el The hyper keratot c masses merge to form a central mass and crater The acanthot c reas merge to constitute an rregular invasion of the cutis. The corium provides stroma and hyper t ophies by digitation of papillae, but stops spontaneously The lesion is destroyed by inflammatory reaction, shown by microabscesses and later scarring

► [The existence of the entity molluscum sebaceum or "keratoacanthoma is no longer questioned. While it resembles prickle cell epithelioma in many ays, it is generally considered as benign growth which tends to heal spontaneously. In these respects, however difficulties sometimes arise In admittedly rare cases in which the clinical and histologic appearance is typical for keratoacanthoma the lesions have been know to recur or develop into prickle cell epithelioma (Beare, Lancet 1 182, Jan. 22, 1955, and Siklerz, Ztschr Haut. u. Geschlkr 19 321 1955) —Eds.]

Aggregated Keratoacanthomas (Mollusca Pseudocarcinomatosa) H W Spier and W Th es (Univ of Munich) report case

Man, 61 m six years had eight keratoacanthomas which spontaneously disappeared within three to four months, leaving small retracted scar There was no connection with seasonal factors or exposure to light or tar and no history of use of arsenical-containing drugs H was seen because of an aggregation f three already confluent, spherical or oblong firm, flesh-colored tumors, with beginning crater formation in the center on the right upper lip lateral and below the scar of the last tumor (Fig 43)

Histologic examination revealed the typical features of keratoacanthoma with epithelial proliferation extending down to sweat gland level and scar formation. Epithelial proliferation and follicular epithelium ere closely connected. During the next weeks and months the lesions showed marked involution, and after 5½ months cicatrization was nearly complete.

Generall three types of pontaneously healing carcinoma l k cutaneous tumors (mollusca pseudocarcinomatosa) may be observed (1) solitary type represented by molluscum

1 Hautarzt 5 306 [illegible] May [illegible]

sebaceum (MacCormac and Scarff) identical with kerato-acanthoma (Freudenthal) (2) a multiple type, i.e., multiple spontaneously healing epithelioma of the skin (Ferguson Smith) and (3) a generalized type.

The present case is remarkable because of the existence of a circumscribed keratoacanthomatosis consisting of at least three aggregated, secondarily confluent and proliferating



Fig 43.—Aggregated keratoacanthoma of three to four weeks duration. (Courtesy of Spier H. W and Thies, W Hautarzt 7:206-209 May 1956.)

keratoacanthomas which healed spontaneously with cicatrization within 5½ months

► [Even with the full knowledge that keratoacanthomas, with rare exceptions, do involute spontaneously in time, it is difficult to stand by while these often rapidly growing tumors involve more and more tissue, in particular around the nose and mouth or elsewhere on the face.—Eds.]

Profuse Keratotic Lentiginosis Occurrence of multiple lentigines in the same person is not exceptional e.g lentiginosis mediofacialis (Touraine) lentiginosis periorifacialis (Peutz Touraine) Generalized lentiginosis, lentiginosis profusa (Darier) however is rare R Degos and A Carteaud[3] (Paris) present a case noteworthy for the generalization and the hyperkeratotic character of the lentigines

Girl 19 noted many pigmented spots in the gluteal region. Six months later they showed an eruption-like spreading without preceding infectious disease, therapy physical or mental shock. On examination, hundreds of lentiginous lesions were seen on the

(3) Ann. dermat. et syph. 83 123-129 Ma Apr 1956.

buttocks, abdomen, arms and legs. Some were flat and smooth, but most were prominent, convex and scaly (Fig 44) From these, a large, thick, lamellous scale could be curetted off which, particularly noticeable on its lower aspect, showed a round pigmented spot. Lesions varied in size (0.1 5 mm. in diameter) and from bright yellow to deep brown or black, showing no signs of malignant degeneration. Around the lentigines, the skin was somewhat ichthy



Fig 44 (Courtesy of Degos, R., and Carteaud, A. Ann. dermat et syph. 83 125 126 Mar Apr 1956.)

osiform, covered by round, translucent, unpigmented scales which could easily be removed.

Histologically the lesions were nevi with the characteristic structure of lentigo and also showed ortho- and parakeratosis. Parakeratotic lesions without nevus cells were also seen.

This case is remarkable in that two types of lesions coexisted, those of disseminated, ortho- and parakeratotic lentigo and others which were aberrant scales with clinically rather ichthyosiform appearance and parakeratotic structure. Whether any connection exists between the parakeratotic scales and the hyperkeratosis of lentigo lesions is uncertain Lymphocytic infiltrates were seen in both types of lesions.

Spontaneous Mammary Carcinoma in Men. Wilhelm Adam Wolfgang Nikolowski and Richard Wiehl[4] (Univ of

Tubingen) report two cases. The condition is not so rare in torrid zones but is seldom seen (0 6-1%) in temperate zones.

CASE 1 —Man, 84 had a tumor of the left breast for one year He had received no treatment, particularly hormone therapy Examination revealed a plaquelike flat tumor in the left mammillary region on removal of thick, yellow brownish, scaly crusts a sharply defined ulcer as large as a finger nail was seen surrounded by a red-brown, firm, slightly elevated peripheral wall. The adjacent skin was stretched, with the formation of radial folds. On palpation, a hard infiltrate, about 6-7 cm. in diameter was movable on the underlying tissues. In the left axilla there was a lymph node larger than a bean. The prostate gland was normal in size. 17 Ketosteroid excretion measured 5 4 mg./100 ml daily and estrogen excretion 75 μg daily The Staub-Traugott (double sugar tolerance) test showed a plateau curve

Histologic study showed carcinoma solidum simplex with partly medullary and partly scirrhous changes in some areas and varying deposits of large bright, Paget-like cells. Testes biopsy showed that spermiogenesis was normal with markedly rare Sertoli cells. Total extirpation of the mammary tumor with Thiersch graft, was done.

Hormone profile —The testes did not show signs of secretory or incretory insufficiency although Sertoli elements were markedly decreased. The prostate gland was not reduced in size. 17 Ketosteroid excretion was not diminished and estrogen excretion not increased. The abnormal curve in the Staub-Traugott test may point to regulatory disturbances in the hypophysis-thalamic region.

CASE 2.—Man 59 noted a pea-sized nodule of the right breast 1½ years previously and had lost 12 kg during the past year There was no history of hepatic disease, prostatic difficulties or hormone therapy Examination revealed on the right breast, medial to the inverted mammilla, a sharply outlined brown red area of erythema, about the size of a half dollar and covered with adherent red-brown crusts. Underneath, a 6×9 cm., firm infiltrate could be felt. It was on the underlying tissues, whereas the covering skin was fixed and stretched and showed radial folds. From there to the lateral and caudal border of the pectoralis major muscle, several firm, pea sized, subcutaneous, slightly prominent nodules were present, above which the skin was movable. A string of similar nodules was palpable along the anterior axillary fold toward the right axilla, in which a hard, isolated lymph node of about cherry stone size could be felt.

X ray examination revealed pleural effusion in the left diaphragmatic sinus and also well defined, pea sized infiltrations in both lungs. The prostate gland was rather reduced. The Abderhalden reaction was positive for the pancreas and testis. The Staub-Traugott test showed a slightly elevated second peak. 17 Ketosteroid excretion was 7.2 mg./day The serum vitamin A level was 2.5 I.U./100 ml. and vitamin E level 1 400 μg./100 ml Study of the

(6) Arch. klin. u. exper Dermat 203 I 14 1956

ejaculate revealed 200 mg. fructose/100 ml. and oligospermia with 64% normal spermatozoa.

Histologic examination revealed a mixed type breast carcinoma (carcinoma solidum simplex and carcinoma adenomatosum tubulare) growing into the lymph spaces, between the collagen bundles and into sebaceous glands. It contained large, bright, Paget-like elements within rete pegs and strands of tumor cells. Therapy consisted of destruction of the hypophysis with subsequent continued medication with 25 mg. cortisone daily for adrenocortical insufficiency. After five weeks, involution of the pulmonary metastases was clearly marked.

Hormone profile.—Although the fructose content of the ejaculate and 17-ketosteroid excretion were about normal, the smallness of the prostate gland and moderate oligospermia were indicative of a somewhat deficient male hormone. Whether the serum level of vitamin A indicated hypogonadism cannot be decided. The serum level of vitamin E was within normal limits (1,200-2,000 μg./100 ml.). The positive results of the Abderhalden reaction, smallness of the prostate and oligospermia certainly point to an endocrine disturbance.

Of these two cases, Case 2, with extensive metastases, showed anomalies of testicular (ex- and incretorial) function and also of the endocrine profile.

► [It would have been interesting to know whether either one of these male patients had acne vulgaris during adolescence. M. R. Lerner and A. B. Lerner (Cancer 6:870, 1953) found that the incidence of acne vulgaris during adolescence appears to be significantly lower among women who develop cancer of the breast than in a control group. It was thought that this might be explained by the relatively low quantities of androgenic substances or relative abundance of estrogenic substances which probably accounted for the lower incidence of acne vulgaris in these women as well.—Eds.]

Cancer of Lip With Special Reference to Predisposing Influence of Sunlight and Other Climatic Factors is discussed by Martti Johannes Hämäläinen[7] (Univ. of Helsinki) as related to an investigation of cheilitis exfoliativa actinica chronica. The study material comprised 125 patients with leukoplakia, 122 with chronic ulcer, 50 with cheilitis and 810 with cancer of the lip, with a control group of 311 normal persons. Of the patients with a positive history of exfoliation 12 were indoor and 309 outdoor workers. Of the controls, only 50 (16.1%) had a history of exfoliation against about 40% of the other groups. Cancer of the lip developed earlier in patients with exfoliation than in those without. Nonspecific cheilitis as a superficial inflammation was demonstrated clinically in patients with a history of exfoliation.

(7) Ann. chir. et gynaec. Fenniae vol. 44, supp. 6, 1955.

The highest incidence of actinic cheilitis occurred from age 10 to 20

Histopathologic changes seen in actinic cheilitis were epithelial thickening acanthosis and tendency to proliferation. Later the same patients revealed development of precancerous features and malignancy was finally demonstrated. Many irritants however in addition to exfoliation from actinic cheilitis operated in production of cancer of the lip. Patients with actinic cheilitis were more or less sensitive to sunlight in general In this series 65 (8%) of the patients ascribed their cancer to previous trauma but in only 7 (0.9%) did this seem possible Other cancers were found in 54 patients (6.7%) Of 239 deaths in the series 31 (13%) were due to cancer other than of the lip which caused 112 deaths Patients with cancer of the lip had a higher tendency to cancer in general than normal subjects.

Results of radiologic treatment were reported as recovery rates in conformity with Dorn

$$RR = \frac{A}{A + D + L}$$

where A is the number of patients alive at the end of the year A_0 the number alive with no evidence of cancer D the number dead within the year and L the number untraced within the year Five year recovery rates were 55.4% for patients primarily admitted for treatment 65.5% for patients without metastases 43% for surgically treated patients with local recurrence with or without metastases and 42% for surgically treated patients without local recurrence, with or without metastases

Identification of Malignant Potentialities of Melanocytic (Pigmented) Nevus is discussed by Bertram Shaffer[8] (Univ of Pennsylvania) In a simple classification of pigmented nevi in which each type is named by the essential cell component the term "melanocytic nevus is appropriate for the pigmented mole Melanocytes at the epidermodermal junction by a process of multiplication and extrusion into the corium called junctional activity cause the common melanocytic nevus and its clinical variations Junctional activity is necessary for development of melanoma from a pre-existing nevus Those melanocytic nevi classified as flat lesions

(8) J.A.M.A 161 1222 1226, July 28, 1956

slightly elevated lesions, elevated lesions with pigmented halos and verruciform lesions are apt to have junctional activity whereas polypoid, dome-shaped, sessile and pedunculated lesions usually do not.

In clinical evaluation of the histologic type of melanocytic nevus, the following should be considered (1) clinical morphology of the lesion (2) age of patient, (3) age and rapidity of development of the lesion, and (4) its association with other similar lesions. The lesions with suspected junctional activity should not have superficial destructive treatment If they are to be treated, they should be excised and examined histologically Malignant melanoma is exceedingly rare in childhood and though much commoner in the adult, is a relatively infrequent malignancy of the skin. On the other hand, pigmented nevi are commonplace, and it has been estimated that each person has an average of 20 melanocytic nevi. The chances of a lesion becoming malignant are about 1 1,000,000 therefore the validity of the dictum of routine prophylactic removal of nevi is questionable Only lesions suspected of junctional activity need be removed prophylactically

To be sure that malignancy is not already present in a nevus at the time of removal, all specimens should be examined histologically This is important because, despite pronouncements in the literature that partial removal of a pigmented nevus causes malignancy no lesion histologically proved benign has ever been recorded as degenerating into a malignant melanoma after partial removal.

► [The last sentence deserves accentuation and repetition —Eds.]

Melanoma of Skin With Special Reference to Histologic Differential Diagnosis, Clinical Picture and End Results of Treatment. According to Gunnar Brandt[6] (Univ of Helsinki) the term nevus denotes a benign tumor with nevus cells th characteristic constituent, whereas melanoma is a malignant pigmented tumor Brandt studied biopsy specimen from 229 adults and 8 children with a preliminary diagnosis of melanosarcoma. Biopsy specimens of nevi from 177 adults and 54 children were also investigated.

When the histologic structure of the nevi was related to age of the patients, a change of the nevi from junctional to

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(6) Ann. chir. et gynaec. Fenniae, vol. 45, supp. 4, 1956.

intradermal type was suggestive. The even distribution of pigment morphologic uniformity of the basal cells of the epidermis and certain histologic findings suggested that nevus cells are derived from the common palisade basal cells of the epidermis

Histopathologic differential diagnosis of melanomas is difficult Brandt found that misinterpretation of pigment granules and lumps not identical with melanin and failure to distinguish between nevus and melanoma were the commonest causes of error Cellular blue nevi appear to run a clinically benign course and have a peculiar histologic picture so they should also be distinguished from malignant melanomas.

Only three instances were observed in which the presence of nevus cells supported the theory that melanomas develop from nevi Most melanomas seem to develop by direct transformation of the epidermal basal cells. Junctional changes in melanomas essentially resemble corresponding changes in nevi but this does not imply that melanomas develop from junctional nevi Apparently the former originate from malignant and nevi from benign junctional changes the two forms are usually readily distinguishable. It is felt that a junctional nevus should not be regarded as precancerous. In melanoma a long history may be due to a latent stage, during which the tumor is clinically and histologically superficial

Brandt studied six boys and four girls aged 14 months to 13 years in whom the final histologic diagnosis was melanoma in six the preliminary diagnosis was nevus. Histologic appearance varied In two fatal cases (in patients aged 14 and 16 months) it was characterized by large coherent clusters of highly undifferentiated cells. The ill defined protoplasm was highly vacuolated hence the tumor tissue appeared loose. The pigment granules between the tumor cells were undoubtedly melanin In a third patient infiltration was present but otherwise clinically and histologically this tumor seemed to be a highly proliferative nevus In a patient, aged 13 the lesion resembled melanomas of adults Tumors of the other patients displayed histologic peculiarities Cells and nuclei were highly polymorphous and giant cells with one or more nuclei were abundant A tendency toward junctional changes and nest formation was discernible The his

tologic picture of these tumors conveyed a definite impres sion of direct transition from epithelial to tumor cells. Although some patients had a short follow up clinically their tumors appeared to be benign

Since true malignant melanomas with a peculiar histologic picture occur in children, the benign melanomas of childhood should be distinguished by a special term. Brandt suggests juvenile melanoma, to include the type histolog ically characterized by presence of giant cells and lesions resembling melanoma of adults

Wide local excision seems to be adequate treatment for superficial tumors and cellular blue nevi In more ad anced cases, it is safest to excise the tumor and its lymphatic ex tensions in continuity Usefulness of prophylactic discon tinuous dissection of regional lymph nodes is doubtful since dissemination by the blood stream is probable and the lymph nodes apparently do not arrest the di seminating tumor cells. Heavy x-ray irradiation is ndicated where sufficiently wide excision is impossibl Excision appears to be adequate for juvenile melanomas, although in the rare malignant mela nomas of children, radical di section is needed.

* [The majority of dermatopathologists with whom w have had an opportunity to discuss this matter re of the opinion that the skin melanocytes are of neuroectodermal rather than epidermal origin.—Ed.]

Diagnosis and Therapy of Melanocytoblastoma are reviewed by J J Herzberg[1] (Uni of Hamburg) with par ticula emphas on the high diagnostic alue of radioactive phosphorus as a tra er method. This method is based on the fact that cells with increased metabol c activity require more phosphorus than cells with normal metabolism. Patients receive 100-150 μc of P^{32} intravenously and re examined three hou s later w th an appropriate Geiger Muller tube. The window f the i strument is sh elded a d except for an open ng i mpenetrabl to radiation F ve hundred mpulses are counted above both the test rea and a collateral normal ski area nd the d fferences in t me are correlated. After dmin stration f P^{32} generally 3-10 mpulses/second were found bove normal kin above warts seborrheic kera toses and nevi, findings w m la In basal cell cancers the ratio of lesion to control s te count was 0.88 1.75 in prickle cell cancers 1.05 1.75 nd n egetat ng types of both

[1] ... Derm ... 1956.

kinds of tumors 2.5-3.85 i e., the same as in melanomas. In 10 cases of melanoma the ratio was between 3 and 5 (maximal 56) Autopsies and histologic examination confirmed the diagnostic value of this simple method. Above some compound nevi a significant ratio of 1.8 was found. Since these soft brownish nevi existed since birth but were located in the vicinity of a primary melanoma or lymph node metastases beginning melanomatous changes may be suspected in such cases. Disadvantages of the method are that a P^{32} increase also occurs in inflammatory and granulomatous tissue and that beta radiation of P^{32} penetrates but a few millimeters of tissue

The therapy of melanocytoblastoma is still under discussion but because these tumors tend to metastasize there is a race for time. Treatment of melanocytoblastoma with already existing metastases is still less satisfactory Progress may be expected not from more and more radical surgical procedures but rather from gradual clarification of pigment metabolism and the pathogenesis of melanocytoblastoma, with an aim at effective chemotherapy

► [A similar study now in progress at the New York Skin and Cancer Unit by Brauer Kopf, Cave and the junior editor has given both false positive and false negative values. In view of these findings we are of the opinion that this method cannot yet be relied on as an in vivo diagnostic method for malignant melanomas.—Eds.]

Hemangioendothelioma. This rare tumor has a variable appearance which may be confused with hematoma angioma and pyogenic granuloma. Hemangioendotheliomas may vary in size from 0 5 cm to 15 cm or more. In the skin they are generally raised well above the surface and may have surrounding satellites Although generally reddish and obviously suggesting their vascular origin they may be flesh colored although usually soft they may be firm There may be bleeding externally or internally after trauma and the overlying skin may occasionally break down The tumors often become attached to subjacent tissues by infiltration. Growth of the tumors is generally steady and slow Metastases are common and may be local or widespread through the bloodstream or less often through the lymphatics. The commonest sites for metastases are the skin lungs, lymph nodes, liver kidneys adrenals pancreas spleen bones peritoneum and diaphragm. After surgical removal there fre-

quently is local recurrence. The course of the disease may be fulminating, as in the following case reported by R. L. Cormie[2] (Glasgow). Most patients live for several years after appearance of the lesion.

Woman, 52, had pea-size to hazelnut-size lumps of one month's duration, noted first on the outer aspect of the right upper arm, then in the area of the right trapezius and in each breast. Many similar subcutaneous nodules appeared on limbs and trunk in subsequent weeks, especially on the abdominal wall. The first lesions were skin colored, but many became bluish red or red and some became firmly adherent to overlying skin. They were occasionally painful and slightly tender to touch. She showed progressive weakness, which necessitated confinement to bed. Thereafter the condition steadily deteriorated, and she died about four months after the first skin changes had been noted.

Biopsy revealed lesions consisting of areas of short plump spindle cells closely packed together with a rich reticular fibrillar stroma. In places blood-filled lumens were present, and around the margins of the lesion in the mammary fat the appearances were of plump endothelial-lined capillaries and spindle cells in a mass of hemorrhage. In places, the appearances were reminiscent of a rather cellular capillary angioma, but the more solid areas lacked the differentiation and were probably indicative of malignant hemangioendothelioma.

The tumors were too numerous for surgical excision when the patient was hospitalized. A test dose of 1,000 r at 140 kv was delivered in one treatment to one lesion, with no appreciable effect. Diethylstilbestrol was also tried in increasing dosage up to 17 mg./day without benefit.

Angiokeratoma: Skin Lesion to Be Considered in Differential Diagnosis of Malignant Melanoma. Angiokeratoma is a rare disorder characterized by vascular and wartlike lesions situated on the extremities, particularly the fingers and toes. The early lesions are pinpoint to pinhead-sized, pinkish, nonelevated spots. Later they become dull red or purplish and the overlying epidermis becomes thickened, forming a smooth horny or a rough and prickly covering. Discrete or assembled into small groups, these skin lesions are usually readily differentiated from melanomas. K. A. Solonen and G. Brandt[3] (Univ. of Helsinki) report on a patient in whom angiokeratoma was treated surgically as a malignant melanoma. Radical excision with resection of the regional nodes was done.

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(2) M. A. Arch. Dermat. 7: 144-48, August, 1956.
(3) Ann. chir. et gynaec. Fenniae 1:[illegible]76, 1956.

Youth 18, had a congenital mole which presented dark purple islets of discrete nodes, 1 3 mm. above the skin and 3×4 cm. in area, on the right forearm (Fig 45) It had recently grown rapidly darkened in color and begun to bleed readily The clinical finding concurred with the picture of melanoma. Although no uniform primary tumor existed, there was a conglomeration of small dark nodes and the brown tinge was absent. Microscopic examination of the tumor revealed in the uppermost layer of the dermis, vesicles of different sizes filled with red cells in many places they seemed



Fig 45. (Courtesy of Salonen, K A and Brandt, G Ann. chir et gynaec Fenniae 45 73 6, 1956.)

to be situated intraepidermally However the vesicles were always surrounded by a very thin layer of dermal connective tissue. Similar but smaller blood vessels were seen locally also deeper in the dermis. In the covering epithelium the horny layer was greatly thickened. Nothing suggestive of a malignant tumor especially of a malignant melanoma, was observed

It is suggested that an adequate local excision biopsy be made of a suspected malignant melanoma before radical measures are taken

► [It is unfortunate but probably unavoidable that benign lesions, at times, are mistaken clinically for malignant melanoma and that radical surgery is done without benefit of histopathologic diagnosis Some surgeons in most cases advocate wide local excision of malignant melanomas with regional node dissection about two weeks later While this reduces the extent of the initial surgery it does not eliminate unnecessarily wide excision of those lesions that prove to be benign.

Where definite doubt exists as to the diagnosis of malignant melanoma, is it not sufficient to do as Solomon and Brandt suggest—that is, adequate local excision first followed by more radical measures if the histopathologic examination shows malignant melanoma?—Eds.]

Cutaneous Leiomyoma. Classification and Report of Solitary Angioleiomyoma. Skin tumors composed principally of smooth muscle cells (leiomyomas) are classified according to derivation as follows (1) multiple cutaneous leiomyomas from arrectores pilorum muscles, (2) solitary angioleiomyomas from the blood vessel walls principally veins and (3) solitary genital leiomyomas from the muscularis sexualis

Classification of Cutaneous Leiomyoma

	Multiple Cutaneous Leiomyoma	Solitary Angioleiomyoma	Solitary Genital Leiomyoma
Symptoms	Painful, tender	Painful, tender	Rarely painful and tender
Site	Trunk, face, extremities	Extremities	Genitalia, nipple
Size of lesions	Small papules to small nodules	Papules to large nodules	Large nodules
Color	Flesh colored or brown or bluish	Flesh colored	Flesh colored
Histology			
Location	Dermis	Subcutis	Subcutis
Capsule	Absent	Present	Absent
Blood vessels	Not increased	Numerous	Few

or muscularis mammillae Each group has clinical and histologic features as shown in the table. Thomas S. Saunders and Thomas B Fitzpatrick (Univ of Oregon) observed a patient with a solitary angioleiomyoma.

Woman, 44, had painful lesion on the left calf for one year. The lesion looked gray and somewhat translucent, measured 1.5×2 cm. and was firm. There has been no recurrence in two years since surgical excision.

Histologic examination showed a small area of normal skin overlying the tumor most of the corium and subcutaneous tissue had been replaced by neoplasm. The tumor was composed largely of blood vessels surrounded by many smooth muscle bundles and fibroblasts The blood vessels were considered veins their muscular walls were greatly thickened. Many vessels showed abundant small round cells with deeply staining nuclei in their adventitial walls. The predominant cell in the tumor was circularly arranged around the vessels and continued its perished trajectory in the vicinity Its nucleus was baton shaped and stained differentially for smooth muscle Fibrous connective tissue made up the balance of the tumor Neurofibrils could not be demonstrated with a Bodian stain.

J A M A Arch. Dermat. 74 :389-393, October 1956.

Since this angioleiomyoma exhibited neither epithelioid (glomus) cells nor neurofibrils it is felt that solitary angioleiomyomas are not a form of glomus tumor

Lymphadenosis Benigna Cutis. A survey based on 143 cases from literature and 8 hospital observations is presented by W Hofer[5] (Zwickau, Germany) Clinically this condition is characterized by small (miliary) or large painless tumors which are prominent spherical of firm or doughy



Fig 46 —Lymphadenosis benigna cutis with multiple lentil sized, firm nodules on cheeks and nose. (Courtesy of Höfer W Arch. klin u. exper Dermat 203 23-40, 1956)

consistency and bluish brown to brownish red. On glass pressure a yellowish brown color remains. The tumors grow very slowly often displaying a tendency to spontaneous involution In about two thirds of the cases the face and head and in one third the trunk and extremities are involved the lower limbs twice as often as the upper Areas of predilection in the face are the cheeks and nose (Fig 46) ear lobes and forehead are also frequently involved. Lesions may be solitary (in about 60% of cases) or multiple (40%) Statistics on age incidence indicate a higher frequency at ages 5-10 years around 40 and between 60 and 70 The condition appears 2-2.5 times more often in females than in males. In the first age group (10-20 years) 82% of patients show solitary and 18% multiple lesions in the second age group (20-50 years) the frequency curve of multiple lesions rises to about 44% and reaches its peak (57%) in the third

(5) Arch. klin. u. exper Dermat. 203:23-40, 1956

age group (50-80 years) These figures illustrate the increasing frequency of multiple lesions with advancing age.

Histologic study reveals cutaneous-subcutaneous infiltrates, which mostly are perivascular perifollicular and periglandular and are formed by a lymphoreticular tissue consisting of lymphocytes, reticuloid cells and a fine fibrillar stroma Occasionally lymphoblastic elements, transition forms to reticuloid cells and giant cells may be found. Vascular changes include swelling and hypertrophy of intima cells, even complete obliteration of vascular lumen. Characteristic are reaction centers (also called function centers," and previously germinal centers") These are round or oval, have a bright center of reticuloid cells and are surrounded by lymphocytic elements plasma cells, mast cells and eosinophils may also be seen. Rarely germinal centers consist of dark, basophilic reticulum cells. However germinal centers are not always seen, which is why some authors differentiate between lymphadenosis benigna cutis nonfollicularis and *follicularis*. The condition is extremely radiosensitive but responds well also to penicillin and arsenicals Prognosis is good. Since, however lymphadenosis benigna cutis has been observed to be a cutaneous symptom of developing or already existing malignancies follow up of pertinent cases for a considerable length of time is indispensable

► [It is interesting that this condition is extremely sensitive to x-rays and responds satisfactorily to penicillin and arsenic

This dermatosis in some cases must be differentiated from the "lymphocytic infiltration of the skin described by Max Jessner —Eds]

Acanthomas Appearing after Eczema. The appearance of small warty lesions on areas of skin affected by eczema is not a common. Murray G Williams[*] reports on four patients with verrucous lesions occurring during eczema. Constitutional eczema was present in three and one had a generalized dermatitis due to allergic sensitivity Each patient received only local treatment consisting of potassium permanganate baths calamine cream, zinc cream or Lassar s paste two were also treated with a paste containing 3% of coal tar and with 0 5 to 1% hydrocortisone ointment.

In each patient many small slightly raised verrucous lesions were observed a few days after the eczematous process had lessened in severity and appeared in one simultaneous

( ) Brit. J Dermat. 68 268 271, July-Aug 1956.

crop The common site was the back and front of the chest, but the lower parts of the forearms and the wrists were also involved in two patients The patients were in the older age group and three of four had in addition numerous seborrheic keratoses The new lesions were distinct from the already existing more deeply pigmented seborrheic keratoses with the stuck-on appearance of their somewhat greasy scale (Fig 47) They were slightly raised above the surrounding skin surface were white or faint yellow and meas-



Fig. 47—Arrow points to one of new verrucous lesions lying beside larger typical seborrheic keratoma. (Courtesy of Williams, M. G. Brit. J Dermat. 68 268-271 July-Aug., 1956.)

ured a few millimeters to 1 cm in diameter Microscopically the typical lesions showed an area of slight hyperkeratosis and acanthosis but not the familiar characteristics of seborrheic keratoses.

After three to six months most of the lesions had disappeared, but a few remained unchanged or became slightly darker and indistinguishable from seborrheic keratoses.

► [In our experience these lesion are not at all uncommon. It appears surprising that they previously have not been studied more thoroughly and are not mentioned in textbooks. They usually are seen in patients over 60 who are recovering from an inflammatory often pruritic, eruption. In some of our cases these lesions, which clinically appear to be indistinguishable from seborrheic keratoses, were associated with fairly severe persistent itching

The occurrence of these lesions largely in areas predisposed to seborrheic keratoses, and largely in patients already presenting numerous seborrheic keratoses, and their clinical resemblance to seborrheic keratoses, makes one wonder if these acanthomas might not represent a Koebner phenomenon —Eds.]

Eccrine Spiradenoma. On the basis of a study of 136 tumors (134 patients) David W Kersting and Elson B Helwig[7] (Armed Forces Inst. of Pathology) define eccrine spiradenoma as a distinct cl nicopathologic entity It must be dis tinguished from dermal cylindroma, syringoma syringadenoma papilliferum and hidradenoma papilliferum.

Clinically the eccrine spiradenoma is a small, discrete solitary freely movable nodule, soft to moderately firm The overlying skin is often blue The tumor is usually paroxysmally painful but may be only extremely tender It is of long duration usually over fi e years, and invariably runs a benign course, attaining an a erage size of about 1.5 cm in diameter Sites of predilection are the upper ventral por tions of the body including the face and extremities. The tumor was not found on the soles, palms, axillae or genitalia. Recurrence is rare unless removal is incomplete.

Microscopically the growth is an encapsulated solid tumor surrounded by collections of normal eccrine sweat glands and ducts and small nerve trunks which closely invest the tumor or with small vessels, penetrate its dense capsular and nterlobular connective tissue septa. The par enchymal pattern has two cell types rranged in winding solid glandular tubules or cords. There are larger central cells, and smaller dark peripheral cells the minor component. Some of the distinct lobules of the tumor may degener ate into a cystic structure Briefly it is an extensive organ oid, benign, neoplastic proliferation of all the cellular and stromal elements of eccrine sweat gland within a firm connecti e tissue capsule. It is suggested that the tumo spirad enoma may arise from quiescent and rudimentary eccrine sweat-gland a lage which, present in the fetus, remained undeveloped and inactive until unknown f ctors comb ned to provide the exciting growth stimulus. There ar periodic acid-Sch ff positive, diastase-resistant substances in the ec crine spiradenoma which are probably mucopolysaccharides and/or glycoprote ns.

On the basis of the specific clinical and pathologic features, it is concluded that the eccrine spiradenoma must be considered a clinical entity Because of the haracteristic spon taneous paroxysms of pain and the excruciating tenderness to minor st muli, often initiating a painful paroxysm, the ec-

(7) A.M.A. Arch. Dermat. 73:199-227, March, 1956.

crine spiradenoma must be added to the brief list of painful dermal tumors which includes the glomus tumor leiomyoma, neuroma and angiolipoma. The best therapy is local surgical removal which, if complete, is curative.

Eccrine Poroma Tumors Exhibiting Features of Epidermal Sweat Duct Unit. Adnexal skin tumors occasionally show structural differentiation resembling one or several components of the pilary complex which comprises hair sebaceous gland and apocrine gland. Structure related to eccrine sweat glands is less commonly encountered. It occurs in adenomas or adenocarcinomas resembling the coil (spirema) or duct (syrinx) of the gland. Hermann Pinkus, James R. Rogin and Perry Goldman[8] (Detroit) describe five tumors related to the eccrine sweat pore inasmuch as they have histologic features of the intraepidermal part of the sweat duct. They propose the term "eccrine poroma" to denote a subgroup of benign solid hidradenomas.

These tumors seen in three women and two men, aged 42-64 were superficial within and closely connected with the epidermis Tumor cells are relatively small and resemble prickle cells in having intercellular bridges They ordinarily contain no tonofibrils or melanin granules except where they reach the surface and form an epidermis-like covering They tend to arrange themselves around cleftlike lumens with cuticle formation. Tendency to true keratinization may be present. Nuclei are of moderate size oval or round, with several small masses of chromatin but without a large single nucleolus If sweat ducts enter the tumor their lining cells merge with its epithelium. Glycogen in the tumor cells and diastase-resistant cuticles were demonstrable with periodic-acid Schiff procedures (Fig 48) All tumors were removed and did not recur

Differentiation from certain* types of seborrheic verruca (seborrheic keratosis verruca senilis, basal cell papilloma) is perhaps the most difficult. Parenchymatous seborrheic verruca, with massive epithelial formations and particularly irritated lesions that imitate intraepidermal epithelioma (Jadassohn) may closely resemble the structure and cell type of eccrine poroma.

* [The authors note that in three of these five cases a melanotic melanoma was suspected clinically.—Eds.]

(8) A.M.A. Arch. Dermat. 74: 511-521, November 1956.

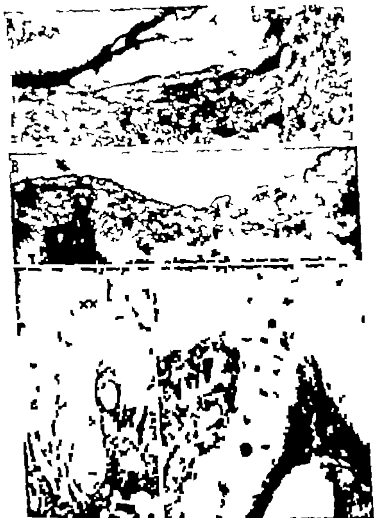


Fig. 48.—Diastase-resistant Schiff-positive material. *A*, dark-staining material in cyst lined by smooth-surfaced tumor cells, some showing thin dark cuticular rim; reduced from ×443. *B*, globules positive-staining cuticle on cells lining another cyst; reduced from ×443. *C*, detail from deep part of tumor with definite duct lumen (*d*) with cuticle and larger cystic lumen (*cy*) above; reduced from ×90. Some cells show fragments of dark-staining glycogen owing to incomplete digestion of this section. [illegible] *D*, casts of positive-staining material in [illegible] spaces); reduced from ×280. (Courtesy of Pinkus, H. et al.: A.M.A. Arch. Dermat. [illegible]:571, November 1956.)

Mucous Cysts of Fingers Report of 26 Cases. O Arner A Lindholm and R. Romanus[9] (Karolinska Hosp Stockholm) observed mucous cysts in 18 females and 8 males, aged 15-81 (average age 53) Multiple cysts occurred in only two Right and left hands were almost equally often involved The second or third finger was the most common site.

In some instances only a fairly diffuse, slight wartlike protuberance is seen in a round area of up to 10 mm. in diam-



Fig 49 —Characteristic mucous cyst of second finger (Courtesy of Arner O et al Acta chir scandina 111 314-321 1956.)

eter This is probably an early phase which later assumes the characteristic appearance a clearly defined round or oval cyst 3 12 mm in diameter usually raised 2 3 mm above the surrounding skin by a sharp boundary The lesion is always on the dorsal aspect of the distal phalanx and usually between the eponychium and terminal joint not communicating with the joint itself (Fig 49) The cyst lies in the skin but is not fixed to the deeper tissues The skin is stretched and is often glossily thin over the cyst Particularly in recurrences the cyst may sometimes show slight reddish discoloration It is translucent markedly fluctuant and commonly slightly tender Pressure does not alter size or shape of the cyst Most patients have a short history and seek medical advice within six months subjective symptoms are slight On rupture or puncture a viscous syrup-like, colorless or yellowish fluid escapes As a rule the cyst develops again within two to four weeks

The cyst evolves by local mucoid change of the collage-

(9) Acta chir scandina 111 314-321 1956

nous substance of the corium—local degeneration or metaplasia. In an early phase the mucoid tissue is diffusely delimited, merging without any sharp boundary with adjacent connective tissue. Connective tissue cells become irregular with mucoid intercellular substance. Later cavities develop surrounded by mucoid tissue, finally uniting to form a large uniform cyst with a fibrous capsule. No epithelial or endothelial lining is present. No inflammatory or vascular changes are found in the vicinity of the cyst and no hemorrhage or trauma. The lesion is not subject to malignant change. Surgery (excision) gives favorable results, but subtotal removal is followed by recurrence.

► [With the exception of not communicating with the adjacent joint cavity the clinical picture and description of these mucous cysts in many ways is similar to that for synovial cysts. We have seen such cysts located close to the eponychium but still communicating with the terminal interphalangeal joint. The question remains whether some mucous cysts are not the same as synovial cysts.

In our hands some cysts have shown excellent response to superficial x-ray given in eight doses of 75 r each, at weekly intervals and also to 340 r closely shielded, repeated twice at two week intervals, for a total dose of 1,020 r.—Eds.]

Pathogenesis of Milia and Benign Tumors of Skin. William Epstein and Albert M. Kligman[1] (Univ. of Pennsylvania) studied milia from naturally occurring lesions on the face and eyelids, those following dermabrasion, those developing in autotransplants of cutaneous tissue and those from cases of epidermolysis bullosa.

Histologically the milia appeared as tiny cysts lined by stratified epithelium a few cell layers thick and contained concentric lamellae of keratin. Origin of these cysts could be traced in every case: each was connected by a cord or sheet of undifferentiated epithelial cells to the parent structure. The epidermis and all its appendages were capable of putting forth strands and cords of undifferentiated or indifferent cells which could potentially give rise to milia. In the naturally occurring facial milia, the undifferentiated epithelial pedicle was derived *principally* from the external root sheath of vellus or peculiar vellus follicles, at that position of the follicular wall from which the sebaceous gland normally originates.

In biopsy specimens of normal facial skin many vellus follicles, whether or not they gave rise to milia, either lacked sebaceous glands altogether or these were imperfect, and

[1] J. Invest. Dermat. 26:1-11, January, 1956.

Mucous Cysts of Fingers Report of 26 Cases. O Arner A Lindholm and R. Romanus[9] (Karolinska Hosp Stockholm) observed mucous cysts in 18 females and 8 males, aged 15-81 (average age 53) Multiple cysts occurred in only two Right and left hands were almost equally often involved The second or third finger was the most common site

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The cyst evolves by local mucoid change of the collage-

(9) Acta chir scandinav 111 314-321 1956.

nous substance of the corium—local degeneration or metaplasia. In an early phase the mucoid tissue is diffusely delimited, merging without any sharp boundary with adjacent connective tissue. Connective tissue cells become irregular with mucoid intercellular substance. Later cavities develop surrounded by mucoid tissue, finally uniting to form a large uniform cyst with a fibrous capsule. No epithelial or endothelial lining is present. No inflammatory or vascular changes are found in the vicinity of the cyst and no hemorrhage or trauma. The lesion is not subject to malignant change. Surgery (excision) gives favorable results, but subtotal removal is followed by recurrence.

[With the exception of not communicating with the adjacent joint cavity the clinical picture and description of these mucous cysts in many ways is similar to that for synovial cysts. W have seen such cysts located close to the eponychium but still communicating with the terminal interphalangeal joint. The question remains whether some mucous cyst are not the same as synovial cysts.

In our hands some cysts have shown excellent response to superficial ray given in eight doses of 75 each, at weekly intervals and also to 340 closely shielded, repeated twice at two week intervals, for total dose of 1,020 —Eds.]

Pathogenesis of Milia and Benign Tumors of Skin. William Epstein and Albert M. Kligman (Univ. of Pennsylvania) studied milia from naturally occurring lesions on the face and eyelids, those following dermabrasion, those developing in autotransplants of cutaneous tissue and those from a case of epidermolysis bullosa.

Histologically the milia appeared as tiny cysts lined by stratified epithelium a few cell layers thick and contained concentric lamellae of keratin. Origin of these cysts could be traced in every case: each was connected by a cord or sheet of undifferentiated epithelial cells to the parent structure. The epidermis and all its appendages were capable of putting forth strands and cords of undifferentiated or indifferent cells which could potentially give rise to milia. In the naturally occurring facial milia, the undifferentiated epithelial pedicle was derived principally from the external root sheath of certain peculiar cell follicles, at that position of the follicular wall from which the sebaceous gland normally originates.

In biopsy specimens of normal facial skin many vellus follicles, whether or not they gave rise to milia, either lacked sebaceous glands altogether or these were imperfect, and

( ) J. Invest. Dermat. 26:1 11, January 1956

showed all transitions from undifferentiated epithelial buds to larger tongues sheets or cords of indifferent cells with a variable degree of sebaceous differentiation or none at all. Frequently at the normal site of the sebaceous duct two epithelial buds or cords appeared which extended out around the follicle and formed a ring of essentially undifferentiated or indifferent epithelial cells Sometimes, the two buds failed to join but grew in irregular configurations. When viewed in the longitudinal axis of the follicle these buds much resembled anlagen of sebaceous glands except for the imperfect and variable degree of sebaceous differentiation and the tendency to disoriented growth Some of these imperfect anlagen clearly tended to keratinize and unquestionably were the earliest beginnings of a milium

Milia do not arise exclusively from follicles. Other portions of the cutaneous epithelium also may provide undifferentiated epithelial cells which may subsequently organize into a milium In the case of epidermolysis bullosa several typical milia clearly derived from the eccrine duct. In autotransplants they arose from the epidermis itself and from the external root sheath

Milia often follow dermabrasion for acne scarring The abrasion when deep extends about halfway down the follicle and frequently causes lobules of sebaceous glands to be cut off and isolated in the dermis These later dedifferentiate and remain as isolated undifferentiated epithelial cell nests in the cutis They can usually join the follicle or the surface and redifferentiate into sebaceous glands but when such a connection is not made, they differentiate into milia.

► [Milia are among the most common skin lesions, but generally have been considered so unimportant that relatively little knowledge has existed regarding their genesis. Epstein and Kligman emphasize the pluripotentiality and equipotentiality of the epidermal structures and stress the fact that milia are not retention cysts.

In the discussion, H. Pinkus noted that there may be two types of milia (1) spontaneous milia, which are not retention cysts but new growths and (2) milia found after trauma, dermabrasion and bullous diseases, which are temporary structures due to a combination of small retention cysts with proliferative tendencies of the epithelium.—Eds.]

Hibernomas, Brown Fat Tumors, rare human neoplasms are discussed by Frederick G Novy Jr (Univ of California) and J Walter Wilson[2] (Univ of Southern California) Although in hibernating animals most of the brown fat is found as two symmetrical elongated masses between the

(2) A.M.A. Arch. Dermat. 73 149-157 February 1956.

scapulas, in human beings it is found only as scattered islands in the same area and along the esophagus, trachea, large mediastinal vessels and perirenally. Microscopically brown fat differs from ordinary fat in that its cells are about half as large, the fat in its cells is multilocular in contrast to the unilocular distribution in ordinary adipose tissue and



Fig. [illegible].—High power photomicrograph of hibernoma, showing multilocular cells with prominent centrally placed nuclei. (Courtesy of Kerry, F. G., Jr., and Wilson, J. W.: A.M.A. Arch. Dermat. 73: 49-57, February 1956.)

the nuclei are centrally placed, spherical and highly basophilic in contrast to adipose tissue cells in which the nuclei are peripheral, flattened and oval. In brown fat, crystallization is rapid, forming fine curved needles. In adipose tissue, crystallization is much slower and forms fusiform plates. Brown fat is unusually rich in phospholipids and in glycogen. Since the loss of lipids in brown fat cells could be prevented by administration of ACTH in hypophysectomized mice normal metabolism of brown fat seems to require adrenocortical activity.

Hibernomas, a misnomer applied to tumors of brown fat, usually occur in the interscapular area, the lower cervical region and the axillae; they occur equally in the sexes. They

are freely movable firm slightly lobulated, nontender and about 8-10 cm in diameter They are often diagnosed clinically as lipomas and are differentiated from other subcutaneous neoplasms by their location high vascularity and increased warmth. *Microscopic section (Fig 50)* shows the lobules separated by vascular connective tissue septa The cells are similar to those in ordinary brown fat, polygonal, with a coarse granular cytoplasm and centrally placed nuclei with prominent nucleoli They are essentially benign tumors Sarcomatous changes rarely develop in these tumors

► [We are grateful to the authors for calling this entity to the attention of dermatologists. While in most instances there are apparently no indications for removing these fatty tumors, the possibility of malignant change must always be kept in mind. This was brought out also in the discussion to the paper by Novy and Wilson.

As is noted in this article the lower cervical region is one of the favorite locations for tumors of brown fat, a tissue which is stimulated by adrenocortical activity Therefore, one might well ask whether brown fat perhaps plays a role in the formation of the buffalo hump in patients under prolonged treatment with large doses of ACTH or corticosteroids.—Ed.]

Sclerosing Lipogranuloma is described by Herman H Sawicky and Norman B Kanof[3] (New York Univ Post Grad Med School and Skin and Cancer Unit)



Fig 51 —Recurrent lesion on left side of scrotum of 6 years duration (Courtesy of Sawicky H H and Kanof N B A M A Arch Dermat 73 264 265 March, 1956.)

(3) A.M.A. Arch. Dermat 73 264-265 March, 1956.

Man, 57 had noted a white streak on the scrotum 10 years earlier (1945) There was no history of trauma or lipid injection. The lesion enlarged slowly and in 1947 was described as half-dollar sized rubbery swelling in the skin of the left side of the scrotum. (Fig. 51) It was excised at this time but ecurred in six months, with subsequent invol ement of the groin. The scrotal and inguinal lesions were resected in 1949 at the same time that left inguinal herniorrhaphy was performed. The same lesion recurred in six months and persisted, with erythema and weeping as result of trauma and secondary infection. Microscopic diagnosis of sclerosing lipogranuloma was made.

The authors had the opportunity of rev ewing a s milar case Sclerosing l pogranuloma is localized idiopathic fat necrosis in the ingu nogenital region It has been postulated that trauma and njection of exogenous l pid material are etiologic factors. Although not always productive of cure, complete surgical removal of the involved tissues s the treat ment of hoice. Cortisone has brought about improvement in some cases.

► [The editors had the opportunity to see this patient whose lesion was puzzling and caused much discussion as to diagnosis. Ther was no intimation in the patient history of any local injection of lipid material that subsequently could have been the cause of the lesion.—Eds]

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6. FUNGOUS INFECTIONS

Onychomycosis Experimental Study X Vilano a, M Casanova and J Francino[4] (Un v of Barcel na) performed 216 experimental inoculations on normal finger nails in 14 subjects. Th following fungi were used Trichophyton schoenleini, T rosaceum T violaceum, T gypseum T ton surans T rubrum, T acuminatum, Microsporum gypseum, Candida albicans, cephalosporium.

Technic.—The material of human origin and from cultures was mixed with honey and applied to the region inoculated with bandage of cellophane and adhesive plaster for 8-15 days. The inoculation as made by simple deposit at the angle formed by the nail groov at the junction between the free margin of the nail and the tip of the finger in half the patients and after superficial scouring ith sandpaper in the others. All inoculations into the free surface of the body of the nail were made after previous scouring with sandpaper

Material was inoculated into the nail bed through the nail b an

oblique cut made with the bistoury after the entire body of the nail had been incised, the knife reached the nail bed as indicated by slight pain. Hemorrhage was avoided in every instance. Incisions were made in various regions of the body of the nail, ranging from the lunula as far as the free margin. Goetz's method, used only once, failed

The uncommon character of onychomycosis is reflected in the fact that experimental inoculations succeeded only in 24% of the cases The susceptibility of different areas of the nail varied markedly Although no lesions were induced in the body of the nail and subungual groove the incidence of induced lesions was 63.3% in the nail bed. The lunula was the most susceptible area when inoculation was made by *incision through the body of the nail* and when the fungus penetrated in the region of the root spreading around the latter Clinically the lesions induced appeared as whitish spots in most instances resembling the forms of leukonychia due to fungi which should be regarded as the initial form of onychomycosis Other cases were characterized by subsequent development of these lesions marked by progressive destruction of the body of the nail as the infected area initially appearing in the lunula approached the free margin (Figs 52 and 53)

In contrast with prolonged duration of spontaneous onychomycosis the disease never persisted beyond 180 days. This may have been due in part to the massive character of experimentally induced infection as the latter is likely to give rise to allergic and immunologic reactions different from those resulting in the case of repeated and slight spontaneous inoculations

Marked variations were observed in the severity of the lesions in a single individual and even in the nails of one hand into which the same fungus had been inoculated.

Direct examination and cultures continued to be positive for fungi in experimentally inoculated nails, so long as lesions appeared as *whitish spots near the lunula* on the other hand cultures started to become negative as the changes approached the free margin and the nail underwent a process of decay the cultures finally being constantly negative for fungi This explains in part why direct examinations are frequently positive in spontaneously infected nails whereas cultures are negative in part as in a small number of cases,

negative cultures may be due to the fact that they are made in medium which do not exclude simultaneous development of contaminants present in large numbers in nails. This problem was solved by using a medium containing actidione,* penicillin and streptomycin in examination of spontaneous and experimentally induced infections of nails.

There seems to be no doubt as to the part played by der-

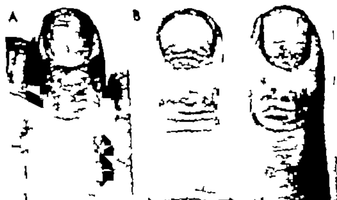


Fig 12 (left) —Inoculation of material from cultures of T. gypseum into supra-ungual groove, resulting in paronychia within 3 days, which disappeared spontaneously after 45 days. In A, remnants of paronychia are still observed within 34 days after inoculation. Transverse band of deep-seated [illegible] starting to appear in most proximal portion of lunula. After 73 days (B) nail shows transversely arranged white bands alternating with dark-colored bands, of rather [illegible] and composed of brittle material. Lesions are due to intermittent attacks of [illegible] growth, intervals exhibiting discontinuous growth of least affected portion of nail.

Fig 13 (right) —Inoculation of material from cultures of T. gypseum through oblique wounds over lunula, extending as far as nail bed. Within 70 days, nail shows wide transverse band, flattened in front of lunula. Body of nail is very soft and crumbles in region of this band. Most anterior band, which passes transversely through entire nail and is very narrow, coincides with line of inoculation. It shows that growth of fungus is obstructed by [illegible] of nail body and can develop only in region of lunula.

(Courtesy of Vilanova, X et al J. Invest Dermat 27 77 181, August, 1956)

matophytes in the pathogenesis, as the clinical pictures induced by inoculation showed constant morphologic features similar to some of those described as occurring in clinical cases. Also the presence of these organisms could be verified in the affected nail and could be isolated by cultures. It was also observed that previous disease of the nail is not essential to development of dermatophytes.

Onychomycosis and tinea capitis have several features in common. Infection is confined to certain areas in the vicinity

of the root possibly because of adequate humidity or chemical composition prevailing in these areas. Like the hair the nail disintegrates as the region involved moves away from the root during growth. Avulsion of the root is indicated in both conditions the root of the hair is removed by epilation and that of the nail by surgical avulsion without which no constant and permanent cure can be obtained.

► [Probably the most daring and certainly one of the most interesting and most informative pieces of work in this year's dermatologic literature. Among the many fascinating findings was that there were only 24% takes" following inoculation in the attempt to produce onychomycosis, that to produce infections it was necessary to inoculate the fungus in the region of the root of the nail and the nail bed and that the duration of onychomycosis produced artificially was at most 180 days.

It is well known to dermatologists that fungous infection can affect a single nail, with sparing of the other nails. This apparent resistance to infection of the other nails may persist for years (even a lifetime) As pointed out by the authors, the infecting inoculation must take place at the nail root. Perhaps this is much less likely to happen than inoculation occurring at the free edge of the nail and contributes to the low incidence of nail infections.

The findings of Vilanova, Casanovas and Francino in deliberate fungous inoculations of the nails are quite parallel to those of Rosenthal and the senior editor and their collaborators in deliberate fungous exposures of the feet (see this YEAR BOOK, pp. 362 and 363) In our experiments on human feet "takes occurred only in a minority of cases and even in those instances it was impossible to recover the fungi from the skin after a short time.—Eds.]

Onychomycosis Nigricans Black Nails is reported by O Schnapka[1] (Univ of Tubingen)

Woman, 56, showed first nail changes in 1953 malaria infection or contact with black staining drugs or chemicals was denied. Nail changes of right index, middle ring and left index fingers consisted in deep black discoloration of lateral edges and of some transverse furrows The surface of the nails was moderately uneven and showed partly transverse ridges. On the free margins of the nails there was slight onychia semilunaris (s c.—Eds.) all involved fingers showed subungual hyperkeratosis.

Scrapings from nails and subungual hyperkeratoses stained with methylene blue showed numerous ound to oval spores, about 2 3 μ in diameter some with a double contour and budding Cultures from scrapings placed in Sabouraud-maltose-neomycin agar revealed, after three to four days, round grayish white penny sized, faintly glistening colonies that showed a central depression after seven to nine days and later a la a like configuration On microscopic examination of hanging drop cultures fine septate mycelia with oval mostly budding spores were seen which were characteristic of Blastomyces dermatitidis. The same cultures 9 10 days after inoculation showed deep brown black, fluffy coin-sized colonies,

(1) Arch. klin. u. exper Dermat 202 45-50 1955

which, during the following 2 weeks, overgrew the blastomyces culture and macroscopically were Alternaria tenuis.

Particles of healthy nails were half embedded in cultures of alternaria and of blastomyces. Nails in the first showed luxuriant growth in tw or three days, were black after four weeks, and became brittle. Nails in the blastomyces culture did not show any mycotic growth. Nails implanted in cultures of Epidermophyton nterdigitale Trichophyton gypseum, T cerebriforme and Microsporum lanosum revealed mycotic growth. Nails implanted in cultures of Candida albicans and Sporotrichum Gougerot did not show mycotic ir olvement.

The coloring material in Alternaria tenuis, fter previous crushing of the culture material was slightly soluble in acetone but barely soluble in water ether benzene and chloroform.

The fast growth of blastomyces and the subsequent over growth with alternaria n culture seem to indicate that in a similar manner in nails, blastomyces is the pacemaker for th weakly pathogenic, black alternaria.

* [It seems unnecessary to assume that the blastomyces acted as pacemaker for the nail infection in this patient, as normal nail was affected hen embedded in culture of Alternaria tenuis without blastomyces being present —Eds]

Trichophyton Rubrum Infections Clinical, Mycologic and Experimental Study Margarita Sil a, Beatrice M Kesten and Rhoda W Benham[8] (Columbia Univ Presbyterian Med. Center) attempt to correlate in T rubrum nfections, was done previously with T mentagrophytes the mycologic haracteristics of a fung us isolate and the cl nical le sion it prod ces Of 70 pat ents with T rubrum nfections tudied clinically all had n ol ement of th nails, but paronychia was ra e The feet nd hands were commonly infected, the lesions ppearing in the following order desqua mation erosion and seasonal maceration of the toe webs rregular del cat collars of overhanging scales with mildly erythematous centers on the glabrous skin of the feet and one hand and noninflammatory hyperkeratosis of the soles nd palms with mildly desquamating erythematous areas xtending nto th adjoining kin Less common lesions ere ridged flexion creases of the palms irregular m ldly erythematous unilateral maculopapular nd follicular patches on the lower extremities erythema nodosum-like lesion on the legs a d dermatitis-herpetiformis-l ke lesions.

C lt e specimens were planted on Sabouraud's glucose agar t which cyclohexamide pen cillin and streptomycin

[8] J Invest Dermat 25 311 326, November 1955

were added Trichophyton rubrum was isolated from one in six cultures in addition some saprophytic fungi and Candida albicans were grown Tests with bacterial filtrates from cultures in which growth of T rubrum was inhibited produced immediate wheals without flares in three of nine patients and a local application brought improvement in the infected nails of two

Mycologically the study of 46 isolates revealed no differences that could be correlated with the lesion from which they came Of the four strains studied in detail one of the isolates from a superficial lesion poor in pigment production proved identical in its nitrogen nutrition microscopic morphology and type of experimental lesion to the isolate rich in pigment production which came from a follicular pustule. When these strains were cultured in autoclaved soil, the poor pigment producer regained pigment and became indistinguishable from the isolate rich in pigment Increase in pigment production was noted after the culture was kept in an incubator at constant temperature for a week and then subjected to a varying temperature for the next week, although the difference in light and oxygen tension under different circumstances might also have influenced this effect.

The inability of dry heat-sterilized soil as opposed to autoclaved soil to support the growth of dermatophytes, may be explained by the longer exposure to a much higher temperature required by the former method, which may have altered the nutrients in the soil. The increase of pigment and sporulation in isolates cultured in autoclaved soil was not accompanied by an increase in virulence, which fact requires further study Culturing T rubrum in autoclaved soil was of value in preventing and reverting pleomorphic changes. Experimental inoculation of the skin of guinea pigs and rabbits was successful Likewise, experimental inoculation of the skin of two patients reproduced the lesions seen in T rubrum infection and its longer duration suggests the absence of acquired immunity

Persistent Fungous Infections of Skin, Hair and Nails are discussed by A J E Barlow and F W Chattaway [7] Two illustrative groups of infections are those of tinea capitis due to the anthropophilic fungi and those due to Trichophyton

(7) Lancet 2 1269-1271 Dec. 17 1955.

rubrum. There are considerable differences between epidemic and sporadic cases, probably based on differences of the host parasite relation. Clinically there are two groups of dermatophytes one attacking the hair follicle, the other the horny layer of the skin and nails. It is believed, though unproved, that fungi can grow only in fully keratinized structures. After pathogenic invasion, the clinical picture is ascribable to damage to the fabric of the skin, hair and nails as the fungus grows through and the host's reaction including epidermal and follicular inflammation, eczematous reactions and hyperkeratosis of affected areas.

To improve treatment in resistant types of infection, it is important to bring the fungicide or fungistatic to the site where the fungus is growing. Breaking the hydrogen links in keratin by urea facilitates penetration. Sodium metabisulfite breaks the disulfide bonds. The cross link between keratin molecules is disrupted by ninhydrin.

Five patients with resistant T rubrum infections soaked one foot in the following solution sodium metabisulfite, 5 Gm phenyl mercuric nitrate, 0 133 Gm. urea 50 Gm., water to 100 ml. with addition of 0 1% calsolene oil. After six hours, soles and nails were kept moist by spraying for two hours with a solution of 2% ninhydrin and 0 133% phenyl mercuric nitrate in 50% ethanol Treatment was repeated in 48 hours. Feet were not washed for one week. Scrapings showed penetration of the outer but not the deeper layer of nail and mycelia were found in the deeper layers. After six weeks, the nails were much better clinically but mycelia were still in scrapings, although the treated foot was much better than the control Penetration was inadequate probably because urea is not a sufficiently strong keratolytic for nails. Fungistatics excreted as mercapturic acids in combination with keratin would be desirable but most available substances are too toxic for this. Further study of the barrier presented by keratin to penetration of fungicides into lower epidermal layers and the lower two thirds of the hair follicles is necessary Increased knowledge of the metabolism of these organisms and factors which determine their parasitism including effects of temperature and humidity and their susceptibility to fungicides is needed.

► [All attempts to approach the problem of "resistant" fungous infections

of the skin, hair and nails on the basis of the principles underlying these studies have failed in the past, as have the authors' trials. There are three principal avenues which can be used singly or in combination to attack these fungous infections (1) topical medication which is capable of reaching and killing each and every fungus, no matter where it is embedded in skin, hair or nail *(all such attempts hitherto have failed)* (2) raising the resistance of the skin, hair and nail so that the fungi are prevented from invading these structures or are quickly destroyed after they invade (many persons appear to have such a natural resistance but the factors which bring it about are largely unknown) (3) systemic administration of fungistatic or fungicidal agents (at present *no compounds are known which are effective when given systemically for this purpose*) —Eds]

Tinea Capitis Due to Trichophyton Sulfureum was observed by J Martin Beare[8] (Belfast) in 45 boys and 37 girls aged 2 14 years mostly from large population centers. A severe inflammatory reaction occurred in 23 slight erythema with mild folliculitis in 15 and no reaction in 44 In three patients the noninflammatory reaction became severely inflammatory after an appreciable delay

Relatively noninflammatory infections were often exceedingly difficult to diagnose Frequently the patches were tiny and only an occasional broken-off hair led to suspicion of ringworm Sometimes purely clinical differentiation between this infection and mild patchy seborrheic dermatitis was impossible Many mild scalp infections due to T sulfureum are probably unrecognized.

Difficulties in management and treatment are considerable. X ray epilation is indicated in extensive noninflammatory cases Watchful expectancy with anticipation of spontaneous cure probably within a year seems the most logical treatment for insignificant and noninflammatory patches. The development of kerion hastens cure

► [It is fascinating to watch the epidemiologic changes which cause epidemics of disease due to one organism to recede and epidemics due to another organism to occur Decrease in the incidence of M audouini infections and increase in T tonsurans or T violaceum infections of the scalp is one example Decrease in T mentagrophytes infections and increase of T rubrum infections of the feet is another Perhaps the present recession in the incidence of syphilis and of scabies, at least in part, is based on *similar* factors rather than being due entirely to improved methods of treatment.—Eds.]

Use of Detergents for Direct Mycologic Examination. G Achten[9] (Free Univ Brussels) prepares scales hairs or nail scrapings with an aqueous solution of 0 1% aminol and 0.2% basic fuchsin in a manner similar to the usual potassium hydroxide mounts but without heating Mounts are ready

(8) Brit. J Dermat. 68 193 199 June 1956
(9) J Invest. Dermat. 26 389-397 May 1956.

for examination in 2 10 minutes The time depends on the nature and thickness of the material. With this method, the clearing of hairs scales and nail scrapings is very satisfactory artefacts are rare. Four basic dyes were tried basic fuchsin nile blue, bismarck brown and janus green. All of them stained mycelium and spores in the presence of detergent but best results were obtained with basic fuchsin. With aminol and a basic dye, direct bacteriologic as well as mycologic examination of the mount was possible.

Study of implantation into Sabouraud's medium of material used in the aminol-basic fuchsin preparations was begun Hairs gave positive results more often than scales Aminol appeared to have antifungal properties, depending on concentration of the surface-active agent and contact time.

► [Aminol is a cationic detergent. The anionic surface-active agents sodium lauryl sulfate and sodium lauryl sulfonate previously have been used for the same purpose (see, for example, Mandel et al J Invest. Dermat. 18 61, 1952) One of the most important practical advances in mycologic technic is yet to be made, namely development of a procedure which permits for speedy identification under the microscope of fungi in scales and hair and subsequent use of the same material for preparing fungous cultures. Results of such in vitro studies as those of Achten lead one to wonder again as to the relative lack of effectiveness of such detergents in aiding the penetration of fungicidal agents in in vivo therapy —Eds.]

Selective Staining of Hair with Tinea by Mercurochrome was tested as a diagnostic method in 40 cases of favus and 27 of tinea capitis by Jean Bonnet and Albert Florens.

Scalp and hair were anointed with a 2% solution of mercurochrome in alcohol which dyed the hair deep red When washed with soap 24 hours later healthy hair regained its natural color hair affected with tinea remained red. Affected hair was easily recognized, distributed in reddish plaques, with patches of healthy unstained hair between them. Microscopically all stained hairs examined showed parasites and all unstained hairs were normal. In some cases diagnosis of tinea could be confirmed by microscopic examination of stained hairs, when all previous examinations had shown no parasites Wood light was not helpful in these cases

► [This demonstration is interesting for practical as well as theoretical reasons. If regularly reproducible and specific for fungous infections it will aid in the diagnosis and treatment of at least certain fungous infections of the hair. What are the changes produced in the hair by the fungus so as to enable infected hairs to react differently to the mercurochrome® stain than noninfected hairs?—Eds.]

(1) Bull Soc franç dermat et syph 61 291 292, Ma June, 1954.

Cutaneous Torulosis is surveyed by Y. Bureau, H. Barrière and R. Trichereau[2] (Nantes) and a case history is reported.

Man, 57, had had, for five months, a group of lesions on his right hand that developed without pain or inflammatory signs. The periungual and adjacent areas of the right middle finger showed a vegetating verrucoid lesion that was covered by bluish red epidermis, slightly scaly in places and of soft consistency. On the back of the hand there was a chain of five nodular similar lesions of various sizes and shapes (Fig. 54). The epitrochlear gland was slightly painful, firm and well-defined. No other cutaneous, neurologic or pulmonary changes existed. McManus stained biopsy displayed round, rose colored encapsulated bodies (diameter 5-12 μ). Biopsy also revealed epidermal atrophy, lymphocytic-histiocytic infiltrates



Fig. 54.—Cutaneous manifestations of cryptococcosis, showing digital lesions. (Courtesy of Bureau, Y., et al.: Ann. Dermat. et syph. 82: 484-509, Sept.-Oct., 1955.)

with giant cell formation and numerous vascular lumens in the middle and deep derma. Within these infiltrates the same bodies were often seen in giant cells. Cultures after 48 hours exhibited numerous, smooth, brilliant, whitish yellow colonies of *Cryptococcus neoformans*.

Hemoglobin level was 40%; red blood cells, 2,210,000; white blood cells, 17,500.

Pulmonary radiography revealed densities in the right lung apex. In the sputum, yeast elements were found that were not cryptococci. Lumbar puncture disclosed albumin 0.30, glucose 0.58, NaCl 7.5, less than 1 lymphocyte. The ocular fundus displayed noticeable paleness.

Cryptococcosis, identical with European blastomycosis, is caused by C. neoformans, a saprophyte of widespread occur-

[illegible] vary

[illegible] port

[illegible] stive

[illegible]

apparatus and skin. Incidence is high in middle-aged men.

(2) Ann. dermat. et syph. 82: 484-509, Sept.-Oct., 1955.

Most constantly the central nervous system is involved, showing meningoencephalitic signs (yeast meningitis) which vary depending on the course—acute, localized or more diffuse. Pulmonary lesions are often associated with changes of the central nervous system systemic involvement is often revealed by autopsy only Cutaneous manifestations occur in only about 10% of cases, and are mostly associated with lesions of the central nervous system or pulmonary lesions isolated cutaneous involvement (as in the case cited) is extremely rare.

Most frequently observed in cutaneous cryptococcosis are rose colored to brownish, noninflammatory painless granulomas of soft, pseudofluctuant gelatinous consistency Papulopustular acneform eruptions are also observed, but ulcerations and pseudoinflammatory tumefactions are rare. In [illegible]ol ement of mucous membranes shows nodular infiltration, ulcerations or granulomatous tissue in all of which cryptococcus is evident. Since cl nical diagnosis is often difficult, the diagnosis must be ascertained by direct examination of [illegible]mears and biopsies, by culture on Sabouraud s agar and by inoculation (intraperitoneally or intracerebrally) in mice rats or guinea pigs. Most con incing are intracerebral findings of cryptococcus after inoculation elsewhere In some cases cryptococci were found in blood and urine Cerebrospinal fluid is often turbid or xanthochromic, showing marked increase in cellular content (200-800 cells) with predominance of lymphocytes increased albumin and decreased [illegible] gar val es.

The course of the disease is either rapid (a few weeks or months) the meningoencephal tic type, or more prolonged (two to four years) in the localized type. With few exceptions, the condition is fatal.

As to treatment, various preparations have been suggested, of which aromatic diamidines (propamidine, stilbamidine) [illegible]d diethylstilbestrol showed promising results. The latter drug used in the above case was followed by no hormonal disturba ces. The patient, however died a few months later of gra cryptogenetic anemia.

Is Cutaneous Blastomycosis a Systemic Disease? Defense of Fading Concept That Cutaneous Blastomycosis Is a Primary Inoculation Process. Warren L. Macaulay[1] (Fargo

(1) A M A Arch. Derm. 73:540 543, June 1956.

N D) reports a case of cutaneous blastomycosis treated successfully with 2 hydroxystilbamidine

Man, 25 acquired a blister on the left great toe from wearing ill fitting shoes. The next day while at his regular work in a grain elevator a door fell on the toe, rupturing the blister The lesion became progressively larger with itchy sensations and after 18 months the patient was hospitalized. Examination revealed a 3.5×2.5 cm. sharply demarcated ulcer with raised edges on the mediodorsal surface of the left great toe near the base. The ulcer was dark red and had a warty surface with numerous papillae which bled easily Potassium hydroxide smears showed thick walled, doubly refractile, yeastlike cells. Cultures from the wound on Sabouraud's medium grew Blastomyces dermatitidis.

The patient was treated with 2 hydroxystilbamidine—110 mg in 200 cc of 5% dextrose in water The dose was slowly increased, until a total of 3.035 Gm. was given. After treatment, the lesion was less thick, losing some of its verrucous appearance and tending to flatten out. Four weeks later it had healed and only a smooth scar remained. Several chest x rays were negative

It has been claimed that blastomycosis is a systemic infection However the local injury the probable infection in the dusty environments of a grain elevator and the absence of pulmonary or other involvement suggest that in this patient blastomycosis was not a systemic disease but a cutaneous manifestation

► [Is there any reason why blastomycosis due to B dermatitidis could not be a primary inoculation process in some cases and a systemic infection in others —Eds.]

Sporotrichosis Special Reference Revision of So-called Sporotrichum Gougerotii is discussed by Arturo Carrión and Margarita Silva[4] in an attempt properly to classify this fungus, isolated from a single subcutaneous lesion of the type usually produced in sporotrichosis The organism has several morphologic characteristics not originally described which preclude its clas ification as a sporotrichum

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successive buddings similar to cladosporium sporulation. On culture, it produces dark aerial and submerged mycelia early growth in some mediums having a moist yeastlike appearance Microscopically it corresponds closely to the black

(4) A M A. Arch. Dermat. 72 523-534 December 1955

yeasts. It has a yeastlike phase and shows sporulation of the pullularia and cladosporium type. It is specifically characterized by production of phialides which bear spores by abstriction at the apex and have no terminal receptacles. On the basis of its morphology it is recommended that Sporotrichum gougeroti be assigned to the genus cladosporium (Hormodendrum) until relations among dematiaceous pathogens are better known.

Folliculitis Barbae Caused by Candida Albicans was experimentally proved in two cases by C Schirren and H Rieth[4] (Univ of Hamburg)

CASE 1.—Man, 64 had parasitic sycosis in 1930 In October 1954 an eruption in bearded areas became worse after treatment with chlortetracycline ointment. The chin and upper lip showed redness, swelling and follicular pustules. Mycologic examination revealed C. albicans in hairs and scales.

CASE 2.—Man, 57 had tuberculosis colliquativa cutis of the left groin since June 1954 Since March 1955 he had an ill defined area of redness, swelling and follicular pustules and few yellowish crusts in each corner of the mouth. C. albicans was found by microscopic and culture examination in hairs and scales.

For culture Kimmig's diagnostic agar was used (peptone, NaCl and glycerin, 5 each glucose 10 standard II nutrient bouillon Merck 15 agar-agar 30 distilled water to 1 000) The agar was sterilized for 30 minutes on three subsequent days. Before cooling 40 units each of penicillin and dihydrostreptomycin were added. Isolated strains were re-examined and kept for eight days in Roulin solution to destroy any possible bacteria

In human pathogenicity tests, self-experimental inoculation on the left forearm with C albicans strain from the patient in Case 1 revealed no changes on the third day and diffuse redness swelling and follicular pustules on the sixth day. Ten days after inoculation the redness was gone but perifolliculitis was still present. Mycologic examination yielded scanty positive findings on the sixth day but ectotrichal growth of C albicans on the fourth day. Bacterial growth was also found after 10 days. Cultures showed C albicans in fluid and tops of pustules as well as around hairs On the 25th day the inoculation area was slightly brownish and covered by fine scales on the 31st day it was sharply defined, hairless and depigmented. To the 26th day C. albicans

[4] Arch klin u exper Dermat 203 377-380 1956.

could still be found but not later because 3% mycostatin-propylene glycol solution had been used for treatment.

For animal pathogenicity tests 10 loopfuls of C. albicans strain in 2 ml. saline were used of which 0.2-1.0 ml. was given intravenously and intraperitoneally to white mice, intracardially to guinea pigs and intravenously to rabbits. All animals except one intraperitoneally infected mouse died within a few days. Candida albicans could be recovered from the kidneys, brain, liver, spleen and heart's blood of the intravenously and intracardially infected animals.

Pathogenicity tests in chick embryos were positive when the allantois was infected. Pure cultures of C. albicans could be recovered from the liver, brain, eyes and kidneys of chick embryos. Vessels of the yolk sac were surrounded by whitish, entangled threads consisting of mycelium, pseudomycelium and blastospores, but not containing chlamydospores.

► [These two case reports indicate an unusual type of involvement due to C. albicans and are noteworthy from the diagnostic and therapeutic viewpoints.—Eds.]

Pathogenicity and Biologic Effects of Candida Albicans on Man and Animals. Observations of Candida granulomas, organic and systemic mycoses have increased considerably since the beginning of the antibiotic era. Pathogenicity and biologic effects, particularly the fermentative activity of C. albicans, have not been fully investigated. Experiments were carried out by K. H. Karcher[6] (Mannheim) with particular regard to the production of exotoxin and sensitizing substances by the organism.

Investigations on C. albicans, apathogenic yeasts and Bacillus [Escherichia] coli revealed that E. coli growth was checked by indigestible yeasts of the C. albicans type. This is practically equivalent to "dysbacteria," i.e., upset of physiologic intestinal balance. After antibiotic therapy the intestinal flora should be normalized by appropriate oral medication. Biologic activities were tested by application of various yeasts to normal human skin. Patch tests with living C. albicans spores showed signs of acute dermatitis after 24 hours with vesiculation following, later changing into a dry eczematoid condition. Candida could be demonstrated in smears and cultures from vesicles. Other yeasts caused less intensive or no reactions.

(6) Arch. klin. u. exper. Dermat. 202:424-448, 1956.

Positive patch test reactions do not indicate pathogenicity but rather biologic fermentativ effects. Candida albicans by its marked proteolytic properties, penetrates easily into tissues and must therefore be considered pathogenic. These ferments are difficult to isolate and can only be shown with living cells. Yeast cells exposed to heat of 70 C. for one hour or filtrates from suspensions of living yeast cells d d not show any fermentative activity Filtrates prepared from liv ing Cand da cells but not containing cellular elements caused, in sensitized persons, a positive intradermal reaction and in healthy persons, a transitory erythema therefore they con tained an antigen c substance. In filtrates from nonpathogeni yeasts, this substance does not exist, since no positive reaction was elicited in sensitized persons It has been found that bacterial autolysates contain glucolipopolypeptides, polysaccharides, nucleoproteins and parvimolecular ubstances that ha e leukotactic and diapedetic ffects, with endotoxins (glucolipopolypeptides) representing more and exotoxins (polysaccharides) less, ffective fractions. S milarly injec tion of pathogenic and nonpathogenic yeast cells causes acute dermatitis du to leukotactic substances. On the other hand, filtrates cause only minor inflammation, which disappears after 24 hours in control persons, but is more marked (ery thema and formation of papules) in person with antibodies to C albicans.

A mal xperiments for determ nation of pathogenicity of yeasts a rejected by Karcher because some animals (rabbit whit mouse) are highly sensiti e, whereas others (guinea pig) are resistant to infection with Candida. Further more for intraperitoneal administration, air or mucin must also be njected Aside from technical shortcomings, results depend on the reactiv ty of the test animals or persons and on quantity rather than virulence of the njected yeasts The horioallantois test is preferred, since the embryo registers t xic effects p ecisely

► [In recent years ther has been tremendous increase in interest in C. albicans and its role in disease in man. For long time it has been known that this organism often is present on skin and mucous membranes merely as part of the "normal" flora It appeared certain that it was by no means an obligatory pathogen and some doubted that it had any pathogenic significance even ben n found as secondary invader It was also known that many persons dev lop specific hypersensitivity of the skin as indicated by positive intradermal test to oidiomycin.

could still be found but not later because 3% mycostatin-propylene glycol solution had been used for treatment.

For animal pathogenicity tests 10 loopfuls of C. albicans strain in 2 ml saline were used, of which 0.2-1.0 ml. was given intravenously and intraperitoneally to white mice, intracardially to guinea pigs and intravenously to rabbits. All animals except one intraperitoneally infected mouse died within a few days. Candida albicans could be recovered from the kidneys, brain, liver, spleen and heart's blood of the intravenously and intracardially infected animals.

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(6) Arch. klin. u. exper. Dermat. 202:424-448, 1956.

In 186 patients with pustular dermatoses long term therapy with tetracycline did not affect the complement fixation test. Those who were seronegative before therapy remained so for as long as 4½ months during therapy. Correlation between the monilia complement fixation test and the incidence or degree of gastrointestinal complaints, e.g. nausea, vomiting cramps, diarrhea or flatus was not apparent. However the positive serologic results and the development of anogenital pruritus were definitely correlated. Of the 27 seropositive reactors, 21 (81%) developed this condition shortly after beginning tetracyclin therapy.

► [The correlation between the positive complement fixation test befor tetracycline therapy and the onset of pruritus and following oral administration of tetracycline has not yet been explained.—Eds.]

Systematic Investigations of Yeastlike Fungi Found on Genital Mucosa were carried out by Georges Garnier[6] (Paris).

Method.—Before and after antibiotic treatment, smears from the vaginal fornix and cervix were inoculated on Sabouraud's medium (2% glucose) to which 750 μg./ml. neomycin had been added and were incubated at 33 C. To identify Candida albicans yeastlike colonies were examined for chlamydospores, using Langeron medium or chlamydospore agar (Difco) on both of which the organisms grow within 4 days or were submitted to sugar fermentation, which takes 10-20 days.

Among 500 patients with various venereal diseases (gonorrhea, cervicitis, syphilis) pathogenic yeasts were cultured in 17.4%, mostly before antibiotic therapy was begun. Of 87 patients in whom pathogenic yeasts were identified, only 3% had clinical moniliasis (whitish, milklike streaks on the vaginal wall and cervix). Neither general (oral or parenteral) nor local (powder or dressings) antibiotic therapy induced general or local complications due to monilia. Findings of yeastlike fungi of the C. albicans type do not imply that they cause the patient's various symptoms. Only seldom were changes on the genital mucosa due to these organisms. This does not exclude possible occurrence of local or general, harmless or serious, monilia infections after antibiotic treatment, but it should be considered in estimating the frequency of such occurrences.

► [These findings once more point out the frequency of infestations with pathogenic monilia without clinical signs or symptoms. Furthermore, it is of particular interest to note that no monilial complications followed the

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Presse méd. 64:884-885, May 2, 1956.

The question of the role of C. albicans in cutaneous disease can now be answered, at least in part. This fungus indeed does play an important role in helping to produce and/or maintain disease in many patients. This is demonstrated by many pieces of evidence, among them the conspicuous response of certain conditions to treatment which is directed specifically against C. albicans, such as with nystatin, for example in the control of genital ping-pong moniliasis among sexual partners. The question of whether C. albicans alone—without preceding other disease or damage—can cause disease or whether it is usually a secondary invader awaits further investigation. Conspicuously little advances have been made in recent years with respect to the immunologic factors concerned in monilial disease.—Eds.]

Serodiagnosis of Moniliasis. Its Value and Limitations. Samuel M. Peck, Rose Bergamini, Louise C. Kelcec and Charles R. Rein[7] (New York) have refocused attention on the complement fixation test as a diagnostic tool in patients suspected of having moniliasis. The controversial historic background of broad spectrum antibiotics in the production of clinical candidiasis is reviewed briefly. Because of the unreliability of the skin oidiomycin reaction, various aspects of serologic reactions have been investigated.

Method.—The best antigen was obtained from Candida albicans isolated from the throat of a child with a fatal case of generalized moniliasis. A suitable antigen could be kept in solution in the refrigerator at 6 C. for months or even years. Monilial cells from Sabouraud's agar culture were collected, washed, centrifuged, dried in a hot oven for six hours, ground to a powder in a mortar, resuspended in sterile distilled water and then passed through a Seitz filter. (Other technics were used, but this gave the most consistent results.) Using the antigen described, the testing technic is similar to that for the serologic test for syphilis with sensitized sheep cells, complement and patient's serum.

The serums of 793 patients with various dermatoses were tested. 686 (86.5%) gave negative reactions, whereas 96 were strongly and 12 weakly reactive, for a total positivity of 13.5%. When duplicates were run, reproducibility was excellent. Of 120 seropositive treated syphilitics 21 (17.5%) reacted positively to the monilia complement fixation test, indicating that this antigen did not contain any Wassermann-reacting lipoidal substances. In contrast, serums were collected from 48 patients with clinical moniliasis of the body folds, of which 34 were strongly and 2 weakly reactive, for a total seropositivity of 75%. There was no correlation between stool culture findings and the monilial complement fixation test in 50 patients.

(7) J. Invest. Dermat. 25:301-310, November 1955.

tion was evident. This reaction appeared 1 11 months after the appearance of the molluscum contagiosum and subsided 1-3 weeks after successful treatment of the lesions. None of the 10 patients had a history of atopic eczema. Patients with atopic eczema in whom an isomorphic irritation effect could be implicated were excluded from this series Contact dermatitis from local therapy was ruled out. This reaction may be due to local sensitization to molluscum contagiosum elementary bodies or soluble products of their metabol sm.

► [It is surprising that such distinct morphologic change (see illustration) observed in this common dermatosis in 10% of the authors cases should hav escaped the trained eyes and inquiring minds of dermatologists for so many years.—Eds.]

Warts Preliminary Survey Virus warts are known to be transmissible and autoinoculable, but little is known of their immunology If the number of warts infecting a patient is related to the ant genic stimulus it might be assumed that many warts should resolve more quickly than single lesions. Investigating this point, A. Barr and R. B Coles surveyed 567 patients with virus warts of these 242 had plantar warts Seborrheic and senile keratoses molluscum sebaceum and molluscum contagiosum were not included. No attempt was made to differentiate the countersunk palmar plantar and subungual and paronychial warts. Most single warts occurred on the feet, whereas multiple warts were most common on the hands The greatest difference between single and multiple warts in relation to site was on the nose, where single warts were about six times more frequent than multiple warts, but the numbers invol ed were small. The ratio of men t women was 1 1.5 About 70% of the patients were aged 5-19 Patients were followed and examined regularly until all the warts completely disappeared.

All plantar warts were treated initially with Thomson s 3% formaldehyd method. All other warts were variously treated with sal cylic acid therapy diathermy and miscellaneous treatments, such as actual cautery CO_2 snow and lush, curettage and x-rays.

In general, duration of the disease increased with the number of warts in each type of treatment. The fastest treatment for up to nine warts was diathermy whereas fo patients with 10 or more warts the time needed for cure was the same

( ) T St. John Hosp. Dermat. Soc. pp. 14-23, Summer, 1956.

administration of antibiotics to these infected patients ("carriers") There can be no doubt, however that a very significant increase in anogenital monilial disease has occurred since the introduction of the wide-spectrum antibiotics. It should be noted in this connection that Garmer apparently did not study the monilial flora of the anal area and the stools in his patients. No matter what the explanation, his findings make it necessary to reconsider the mechanism producing vulvar and perianal monilial infections which follow the use of the wide-spectrum antibiotics.—Eds)

7 OTHER INFECTIONS INFESTATIONS

Eczematous Reaction Associated with Molluscum Contagiosum. Descriptions of complications of molluscum contagiosum have usually been concerned with infection beneath the lesions or an acute sterile inflammatory reaction.

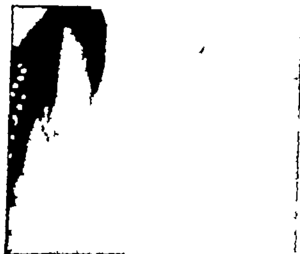


Fig. 55.—Eczematous reaction surrounding molluscum contagiosum papule (Courtesy of DeOreo, G. A., et al. A.M.A. Arch Dermat 74:344-348, October 1956)

An eczematous reaction was observed by G A. DeOreo, H H Johnson Jr and G W Binkley[9] (Cleveland) Among 95 patients with molluscum contagiosum 10 had a localized eczematous reaction surrounding one or more of the molluscum contagiosum lesions This eczematous area was usually 3-10 cm. in diameter and had a sharp margin (Fig 55) The skin in the involved area was edematous, brownish red and covered with small superficial scales No gross vesicula

(9) A.M.A. Arch. Dermat. 74:344-348, October 1956.

Pyramidon was ineffective sympatol* and cardiazol were given. Rapid deterioration, delirium and incontinence followed, and he died on Jan 25 1954

Hemograms obtained on Jan. 19 and Jan. 25 1954 showed hemoglobin 110 and 115% red blood cells 5,300,000 and 5,750,000 and white blood cells 8,100 and 6,800 There were 6% plasma cells and 2% erythroblasts.

At autopsy hyperplasia and hyperemia of tracheal, axillary and inguinal lymph nodes were found. Slight fibrinous perisplenitis and hyperplastic splenic pulp were present. Catarrhal bronchitis with multiple subpleural hemorrhages, fibrinous pleurisy of left lower pulmonary lobe with hydrothorax and pleuritic adhesions of the right side were found. The heart showed brownish discoloration (lipofuscin deposits) and dilatation of the right side minor lipoidosis of coronary arteries and aorta existed. There were hyperemia and parenchymatous degeneration of liver and kidneys. Minor catarrhal gastritis, macular hyperemia of intestines and pancreas, hyperemia of the inner parts of adrenal cortex, edema and hyperemia of the brain and meninges were found.

Microscopic study of cutaneous lesions revealed marked epidermal necrosis with more or less dense growths of gram-positive cocci or bacilli. Cutis of the excoriated areas showed similar changes. Vascular hyperemia and perivascular lymphocytic-histiocytic infiltrates were found. Epithelial elements, particularly of the stratum germinativum and stratum granulosum, often exhibited formation of para or perinuclear vacuoles in the protoplasm, occasionally with eccentric displacement of the nucleus. Findings typical of cutaneous changes in herpes simplex infection were missing. Hyperplasia of lymph nodes was caused by swelling, augmentation and differentiation of reticulum cell elements in sinuses and lymphatic tissues. Cells described as monocytoid, lymphoid cells atypical hyperbasophilic mononuclears immature plasma cells lymphatic plasmoblasts, and lymphatic plasma cells were also found in capsular cens of lymph nodes and other organs. Observed also in viral infections (virus pneumonia, German measles, mononucleosis infectiosa) these cells are often called "virocytes" but are also seen in other infectious diseases (pertussis, polyarthritis, septicemia) lymphogranulomatosis, liver cirrhosis and serum sickness.

Histology of the central nervous system did not reveal any important changes in particular those of herpes encephaliti were missing

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with salicylic acid and diathermy The difference in length of treatment for single and multiple warts was appreciable in both these methods but there was no noticeable difference with the miscellaneous treatments Because the treatments were combined, this observation is of doubtful value. Compared with other treatments salicylic acid and diathermy reduced the time for cure of single warts.

Analysis of single and multiple warts by time taken for cure and duration before treatment revealed no evidence that the more warts a patient has and the longer their duration, the easier they are to cure About half the single warts existed for more than one year before treatment against two thirds of multiple warts Multiple warts take longer to cure and their previous duration is greater

► [*Knowledge gained from this type of study regarding the natural course of warts is essential for proper evaluation of results obtained with suggestion and certain other forms of therapy for warts.—Eds.*]

Herpetiform Eczema with Fatal Outcome is reported, and the condition (Kaposi s varicelliform eruption) is discussed by J J Herzberg and G Pliess[2] (Univ of Hamburg)

Man, 37 had had occasional attacks of asthma and recurrent neurodermatitis since he was 11 years old. First hospitalization was on Nov 16, 1953 because of deteriorating endogenous eczema combined with asthma attacks. Laboratory findings were of no significance except for 12,300 white blood cells and 17% eosinophils. Discharged on Nov 27 1953 he showed improvement of the remaining neurodermatitis patches (face neck, upper chest, back, antecubital and popliteal fossae and dorsa of both hands) On Jan. 17 1954 there was sudden deterioration of the general condition temperature was 100 4 F On the right side of the neck below the mandibular angle was a half-dollar-sized group of vesicles and in the neck region there were several pinhead sized, round epithelial defects (excoriated vesicles) His wife showed remnants of herpes labialis.

On June 19 1954 he was again hospitalized because of the rapidly spreading vesicular eruption. He had redness and swelling of the skin of face, neck, chest and upper back with isolated, markedly dimpled vesicles and partly confluent, partly isolated, dry miliary epithelial defects. Temperature was between 102 and 104 F anorexia and headaches were present Despite oxytetracycline orally (1 Gm./day) and topically the upper and lower eyelids (with the corneas remaining free) upper arms antecubital fossae, dorsa of hands, wrists, popliteal fossae and abdomen became involved during the ensuing days. Vesicles dried so fast and the crusts fell off in such quantity that in large areas dry epidermal necrosis prevailed.

(2) Frankfurt. Ztschr Path. 66 330-347 1955

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form eczema important because of the high mortality (27% in children to age 3 years 15% in adults) can be ascertained by demonstration of herpes simplex virus in the vesicles, increase of neutralizing antibodies in the patient's serum and histologic findings (virus giant cells inclusion bodies in epithelial elements of skin and mucous membranes) In the case described herpes simplex virus could not be ascertained, probably because of the rapid course of the disease encephalitis was not present. However the remarkable changes in regional lymph nodes changes of the hemogram (relative leukopenia terminal absolute granulocytopenia, relative erythrocytemia) indicate to some extent the viral etiology of the fatal disease.

► ["Disseminated cutaneous herpes simplex virus infection superimposed on atopic dermatitis is a much more accurate and therefore preferable name for this important entity Fortunately the syndrome in many cases takes on a much milder form than in the patient described in this article. Often the disease is confined to very limited areas and clinically is not associated with severe systemic manifestations.

Among other forms of treatment which could be instituted in such cases are injections of gamma globulin and whole blood transfusions.—Eds.]

Eczema Vaccinatum With Vaccinial Lesions Strictly Confined to Eczematous Patches is reported by Luis F de Salles Gomes (Instituto Adolfo Lutz) Orlando Natale Bassoi and Luis Dias Patricio[1] (Univ of São Paulo) Vaccinial pustules were localized to the eczematous areas in contrast to previously published cases in which they were also found around the patches or even developed into generalized vaccinia.

Boy 2, had had marked inflammation of chronic eczematous patches on the backs of his knees for five days. Two days later purulent vesicles 5-6 mm. in diameter appeared in both popliteal regions, and he had a septic temperature He had had infantile eczema since age 3 months. In each popliteal region was a well demarcated infiltrated eczematous patch with numerous confluent umbilicated greenish yellow pustules (Fig 56) An erythematous halo surrounded both patches. A hard painful lymph node was palpated in each crural region. Treatment was topical and symptomatic. Recovery was uneventful. His mother had been vaccinated against smallpox 15 days before the onset of his present eruptions.

Samples taken from pustules were cultured on the chorioallantois of 10 day eggs. Typical vaccinia virus lesions grew on scarified rabbit cornea after inoculation with a broth suspension of the virus culture. Typical intracytoplasmic inclu

(1) Lancet 2 1275-1277 Dec. 17 1955.

son bodies were seen in a biopsy specimen of a vesicle taken on the fourth day An antivaccinia hyperimmune rabbit showed no lesions on skin and cornea after inoculation by scarification with the virus isolated from the patient's right



Fig. 14.—Typical patches of eczema vaccinatum. (Courtesy of de Salles-Gomes, L. F., et al. Lancet 1275 1277 Dec 17 1955)

leg A neutralization test on the chorio-allantois with pooled hyperimmune rabbits serums showed a decrease in number of lesions compa ed t the controls.

The hild had scraped the mother's vaccinia pustule, but it s unl k ly that the portal of entry was by local inoculation beca se lesions appeared on the eczematous patches simultaneou ly The trict l m tation of vaccinial lesions to the eczematous pat hes and the mode of development and spread uggest hematogenous dissemination of the vaccinia virus, wh h probably entered the body through the espiratory tract Demo stration of a viremic phase in human variola nd dene of the hematogeno s origin of general accinial sk lesion are confirmatory evidence of the pathogenesis of ec ema accinatum.

* [An interesting, instructive and ell investigated case. Perhaps the authors are correct in assuming hematogenous spread of the vaccinia virus

infection. In our opinion, however, the possibility also must be considered that the simultaneous involvement of both popliteal spaces with limitation of the eruption to the areas of a chronic infantile eczema may be due to the child's scratching of the affected areas with contaminated hands.—Eds.]

Vaccination for Recurrent Herpes Simplex Infection: Initiation of New Disease Site Following Use of Unmodified Material Containing the Live Virus is reported in two cases by M. Paul Lazar[4] (Chicago). The first patient, a man, 22, had had five monthly recurrences of a vesicular crusted eruption of the shaft of the penis within six months, with no history of sexual exposure. Multiple puncture vaccination of the abdominal wall was performed with material from a vesicle. A typical eruption of herpes appeared for 11 of the next 13 months on both the penile and abdominal areas. The second patient, 32, had had recurrent attacks of herpes simplex on the shaft of the penis four to six times a year for the preceding seven years. Smallpox vaccinations were ineffective, as were antibiotics locally and systemically, x-ray and snake venom therapy. After multiple puncture vaccination on the left forearm with fluid from a penile vesicle, the patient had typical herpes simplex eruptions on both penis and left forearm areas five times in 15 months. No benefit from the procedure was noted. The hazard of establishing a new site for recurrent herpes simplex infections must be considered.

► [A very interesting series of events which makes one wonder why instances of involvement of multiple sites with recurrent herpes simplex are not seen more often except under the special conditions prevailing in disseminated cutaneous herpes simplex virus infections (Kaposi's varicelliform eruption). Apparently the virus of herpes simplex is not easily picked up by fingers or finger-nails from the herpes lesion or is not easily inoculated into other body sites.

There may be very great *local* differences in susceptibility to this type of infection, similar to the differences observed in fungous and bacterial infections.—Eds.]

Disseminated Herpes Zoster Complicating Chronic Lymphatic Leukemia: Report of Case with Electron Microscope Study of Vesicle Fluid is made by Gerald P. Rodnan and Geoffrey W. Rake[5] (Brooklyn).

Man, 57, was hospitalized with a history of chronic lymphatic leukemia of 10 years' duration. He had noted progressive weakness, anorexia and weight loss. There was no history of herpes zoster or varicella. Physical examination revealed several petechiae on the chest, generalized enlargement of lymph nodes and hepatosplenomegaly. Hemoglobin level was 7.5 Gm. and the white cell count 126,000 with 96% lymphocytes.

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(4) A.M.A. Arch. Dermat. 73: 70-71, January, 1956.
(5) New England J. Med. 254: 472-474, Mar. 8, 1956.

The patient was given three blood transfusions. On the 11th hospital day vesicles appeared on the right chest wall, additional lesions soon grouping in the distribution of the 9th thoracic spinal nerves. On the fifteenth day he was placed on chlortetracycline, and four days later a rash appeared on the face, arms and chest. These lesions began as erythematous macules, soon surmounted by vesicles filled with clear fluid, which proved sterile on routine bacteriologic culture; many of the vesicles became hemorrhagic and secondarily infected with pyogenic staphylococci. The eruption spread rapidly to cover the entire body surface, including the palms and soles, but there was no involvement of the mucous membranes. At the site of the original herpetic patch there was necrosis of the epidermis. Biopsy of a vesicle from the upper extremity revealed characteristic Lipschütz intranuclear inclusion bodies, with focal accumulation of lymphocytes in the dermis.

The patient's temperature was now 103 F. Blood cultures on the twenty-second day were positive for Staphylococcus aureus and Pseudomonas aeruginosa. The fever was little affected by penicillin. Signs of meningeal irritation developed. The spinal fluid, which was clear with 34 lymphocytes/cubic millimeter and a total protein concentration of 100 mg./100 ml., was sterile on culture. At the end of the fourth hospital week, with the temperature rising to 104 F., penicillin was supplemented with streptomycin and chlortetracycline. The fever cleared, with accompanying clinical improvement. Skin lesions regressed rapidly, leaving only faintly pigmented scar. The patient died suddenly on the 121st hospital day.

Fluid collected by capillary tubes from widely separated vesicles on the extremities and trunk when the varicelliform eruption was at its height was found, under the electron microscope, to contain particles similar to the elementary bodies of herpes zoster in size, shape, central depression and inclusion of some of the bodies in sticky matrix.

It is suggested that in herpes zoster with varicelliform eruption the same virus is responsible for both primary zonal lesion and subsequent disseminated rash and that such an illness may therefore be properly designated as generalized or disseminated herpes zoster.

Atypical Form of Chickenpox with Varioloid-like Rash: Presentation of Case with Laboratory Confirmation of Diagnosis

made by Juan J. Angulo, Luis F. de Salles-Gomes and José Temistocles A. Tartari (São Paulo, Brazil)

Youth, 18, had atypical form of chickenpox with varioloid-like rash 46 days after smallpox vaccination. Less than three dozen discrete vesicles and pustules were scattered on the legs, arms, buttocks and shoulders, and there was one vesicle on the neck. Neither distribution nor individual characteristics of lesions were typical of chickenpox. Most vesicles resembled typical smallpox ves-

icles a few pustules were identical with the umbilicated pustules seen in antismallpox vaccination and generalized vaccinia.

Two biopsies of vesicles showed the classic histologic and cytologic picture of chickenpox vesicles. This diagnosis was supported by negative results of repeated inoculations onto chick embryo chorio-allantois with four samples of lesions, recent successful antismallpox vaccination and clinical data. The last did not support a diagnosis of herpes zoster or herpes simplex. There was no microscopic evidence that the lesions corresponded to nonspecific or specific lesions of Hodgkin's disease, from which the patient was suffering before the rash started.

Complement Fixation in Cat Scratch Disease Employing Lygranum® C.F as Antigen is evaluated by Charles Armstrong Worth B Daniels Frank G MacMurray and Horace C. Turner [7] Lygranum® C F is a commercial antigen prepared from venereal lymphogranuloma virus which fixes complement in trachoma psittacosis, venereal lymphogranuloma and several types of pneumonia but does not differentiate among them It is believed that a positive reaction in a serum dilution greater than 1 5 has significance and indicates that such serums contain antibodies capable of combining with one or more antigenic components found in lygranum® However it cannot be assumed that such antibodies in cat scratch disease are caused by this infection

In 40 patients with clinically typical and skin test positive cat scratch disease the following results were obtained. Of 12 aged 2 24 1 (8 3%) gave a positive reaction in 23 aged 32 73 there were 7 (30 4%) positive reactions 5 patients of unknown age failed to fix complement With the use of the same examination technic in 71 persons with no known attack of cat scratch disease there were 2 (5%) positive reactions among 40 control patients aged 4-25 and 6 (19.3%) among 31 aged 32-68. One had a history of psittacosis 25 years earlier The low titered complement fixation reactions appear related more to the patient's age than to the presence of cat scratch disease Thus the positive reaction to lygranum® C F antigen is without diagnostic value in the individual case of cat scratch disease and affords no evidence that the disease belongs to the psittacosis lymphogranuloma group

Tuberculous Vasculitis with Clinical Appearance of Livedo Racemosa is described by J J Herzberg and K H

(7) J.A.M.A. 161 149-150, May 12, 1956.

Scholz[1] (Univ of Hamburg) in two patients. In contrast to functional types of livedo (e.g cutis marmorata or livedo calorica) persistent livedo racemosa shows endarteritis obliterans with semilunar or eccentric narrowing of the lumen of small arteries in the cutaneous-subcutaneous border and in the subcutis. The pathogenesis of livedo racemosa was explained by a reduced propulsive force during systole (due to the arteriolar vascular changes) and consecutive diminished propulsion of the blood stream in papillary vessels during diastole, with stasis resulting in involved areas. Clinically livedo racemosa appears as livid, often slightly raised, bandlike stripes with branching ramifications (Ehrmann) An additional factor a constitutional tendency to angiospasms, has to be assumed in livedo racemosa. Idiopathic and symptomatic forms of the disease have been described. In the former which mostly occurs in young women up to age 30, endarteritic changes were caused by syphilis severe perniosis cardiac and aortic diseases tuberculosis, particularly tuberculosis cutis indurati a, and infectious diseases unilateral livedo racemosa was observed in patients with circumscribed cerebral disease. Symptomatic livedo was seen in patient with dermatomyositis, acrodermatitis chronica atrophicans polyarteritis nodosa, endarteritis obliterans (Winiwarter Burger) aortosclerosis, alcoholism damage due to arsphenamine, rheumatism and others.

CASE 1.—Girl, 17 had pulmonary disease during infancy the mother died of pulmonary tuberculosis. During the past four to five years, the patient had tendency to cold, clammy hands and feet. Bluish macules appeared on the legs and feet first in 1953. On examination she showed macular reticular condition of the skin on the legs, knees and thighs. X-ray examination revealed calcifications of the *right pulmonary hilus*, increased markings in the left and right upper lobes and densities in the lower right lobe. The Mantoux test (1 1,000,000) was positive. Histologically lymphocytic-histiocytic infiltrates were seen around dilated papillary capillaries, with endothelial nuclei projecting button-like into the vascular lumen. I the cutis-subcutis no specific granulomas were evident, but some arteriolae revealed marked intima proliferation and increased nuclei of muscle cells. Occasionally narrowing even occlusion, of the vascular lumen existed. Mycobacterium tuberculosis was found in Ziehl-Neelsen stained material from biopsy specimens and in cultures.

CASE 2.—Woman, 33, with negative history of tuberculosis, in 1953 first had li id, indurated nodules of the right leg Examina

[1] Hautarzt 5 443-448, October, 1954.

tion revealed hazelnut-sized, firm, mobile lymph nodes on the left side of the neck. The hands, feet and forearms were livid, cold and clammy. On the distal parts of both legs were hazelnut to cherry sized livid, hard, cutaneous-subcutaneous nodules which were not painful on pressure. In addition a livid, partly macular partly reticulated, noninfiltrated skin pattern was present. A chest x-ray showed calcified densities in the right hilus. The Mantoux test (1 1 000 000) was positive. Biopsy revealed epithelioid cell granulomas in the cutis-subcutis region with massive central necrosis, infiltration of the septa of the panniculus adiposus and heavy vascular destruction. Arterioles that were still preserved showed considerable proliferation of the intima with newly formed collagen fibers and elastic lamellae broadened, frayed elastica interna and an increase of cellular elements in the media. Occasionally splitlike narrowing of the vascular lumen was seen.

In both cases, tuberculous endarteritis existed which clinically had the appearance of livedo racemosa. In the second case in which erythema induratum and livedo racemosa coexisted the latter represented the symptomatic type of persistent livedo racemosa

Pathomechanism of Tuberculosis Indurativa (Bazin) The tuberculous etiology of erythema induratum (Bazin) was established long ago but the pathomechanism of the disease is still under discussion. The combined action of several factors is held responsible for the existence of disseminating tuberculous processes in various organs (lymph nodes lungs, bones joints male sex organs tuberculosis cutis luposa papulonecrotica and lichenoides) together with disposing factors which facilitate the nidation of tubercle bacilli in the vessels of the legs or arms e.g. ovarian and particularly thyro-ovarian dysfunction with lowered estrogen level and consecutive vasomotor disturbances. N Simon I Gavallér and S Suranyi[9] (Univ. of Debrecen) studied the role of genital tuberculosis, particularly tuberculous endometritis in the pathomechanism of Bazin s disease

In 39 patients with tuberculosis indurativa (Bazin) all data (anamnestic symptoms results of clinical and laboratory examinations) referring to an existing or preceding genital tuberculosis were collected. It was seen that genital tuberculosis could be excluded in the first group of four patients in whom for other reasons (carcinoma of the cervix, myoma of the uterus, chronic metritis and ovarian cyst) internal sex organs were removed and did not show any tuber

(9) Hautarzt 7 253-257 June 1956.

culous changes and in a second group of six and a third group of eight patients because of coexisting or subsequent pregnancy since active genital tuberculosis precludes preg nancy I a fourth group (11 patients) genital tuberculosis could be excl ded by histologic examination of curetted ma terial and by microscopic-cultural examination of intermen strual secretion and of menstrual blood. In a fifth group (s x patients) curettage material was examined only microscopically Results were negative in all cases and therefo e ex cluded the existence of tuberculous endometritis and most probably also th t of tuberculous infected adnexa, especially since three patients had been pregnant shortly before the ppearance of Bazin s disease three were not married and two of th latter were still virgins. In a sixth group (fou patient) Bazin s disease appeared 14 15 28 nd 29 years after the menopause which excludes tuberculous endometritis or gen tal tuberculosis as the source of tuberculous dissemination t the time Bazin lesions appeared.

Of 110 patients with genital tuberculosis *scars following* lymphomas of the cervix were seen in two patients and tuberculosis papulonecrotica lupus erythematosus and Bazin disease ea h in on patient.

Accordi g to these findi gs no major significance is at tributed to genital tuberculosis and tubercul us endometritis in the pathomechanism of Bazin s disease. The authors rather ssum that in both, erythema induratum and genital t berculos wh ch re d e to hematogenous dissemination f tuberc l bacilli neuroendocrine disturbances play an m porta t part, e.g hyperthyreosis genital hypoplasia, oligo- d menorrhea and leukorrhea on the one hand and kerato- p laris, hypertri hosis and erythrocyanosis of the legs in young women the other With these existing aforemen tioned conditioning factors, circulatory di turbances and pr longed ta ding turn into predisposing f ctors, which f cilitate the idation of tubercle bacilli, with changes of erythema d ratum afterward.

Value of Calmette Vaccine in Prophylaxis of Leprosy \ Pardo-Castelló Francisco R. Tiant and Ramón Ibarra l erez tudied 22 children with negative Mitsuda reactions, originally mmunized with fresh Calmette-Guerin vaccine

( ) Bol. Soc. cubana dermat. sif. 12:144-152, September 1955.

tion revealed hazelnut-sized, firm, mobile lymph nodes on the left side of the neck. The hands, feet and forearms were livid, cold and clammy. On the distal parts of both legs were hazelnut- to cherry-sized livid, hard, cutaneous-subcutaneous nodules which were not painful on pressure. In addition, a livid partly macular partly reticulated noninfiltrated skin pattern was present. A chest x-ray showed calcified densities in the right hilus. The Mantoux test (1 1 000 000) was positive. Biopsy revealed epithelioid cell granulomas in the cutis-subcutis region with massive central necrosis, infiltration of the septa of the panniculus adiposus and heavy vascular destruction. Arterioles that were still preserved showed considerable proliferation of the intima, with newly formed collagen fibers and elastic lamellae broadened, frayed elastica interna and an increase of cellular elements in the media. Occasionally splitlike narrowing of the vascular lumen was seen.

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(9) Hautarzt 7:253-257 June, 1956.

no gonococci. Treatment was as in Case 1 except that ACTH was given intramuscularly every six hours for seven days then gradually reduced. There was immediate response and rapid involution of lesions.

It is suggested that keratosis blennorrhagica is an allergic manifestation of a gonococcic infection. Permanent rem s sion in the disease induced by ACTH confirms its allergic nature

► [A ery interesting response to ACTH, but one which does not necessarily indicate that keratosis blennorrhagica is the result of an llergic response of the skin to the gonococcus.—Eds.]

Skin Infection with Salmonella Rostock in a Newborn Infant. Skin infections caused by salmonella organisms are ex tremely rare During the neonatal period salmonella infec tions are usually caused by fecal contamination from the mother even f intrauterine transmission is pos ible. Pemphigus neonatorum is generally caused by Staphylococcus pyogenes, but streptococci may also be responsible Rolf Lund trom (Stockholm) reports pyoderma, resembling pemphigus eonatorum in an infant aged 1 week with para typhoid fever Before and during deli ery the mother had marked symptoms and signs of enteritis S. Rostock was isolated from feces of both mother and ch ld Both staphylococci of apathogenic type and S Rostock were recovered from the content of the child esicles The skin lesions dried up in a few days and healed without antibiotic therapy

Pos ibl contamination by bacteria on th skin was considered, and the greatest car was used i taking samples. Though t cannot be posit ely ruled out, despite these precaut ons, that th salmonella organism we e deri ed from fecal contam nation f the skin this seems unl kely Th ch ld wa d l ered at the peak of the mother s illness, and it k n thus came into the losest contact with infectiv matter part cula ly fa orable condit ons fo a skin nfection therefor exi ted

► [A s pointed out by the author contamination of the skin with microorganisms from the feces cannot be ruled out entirely Nevertheless the evidence strongly suggests salmonella as the causative organism of the cutaneous lesions One wonders what percentag of cases of pemphigus neonatorum in general is caused by organisms other than staphylococci or streptococci —Eds]

Cutaneous Amebiasis Report of Two Cases with One Autopsy C t neou amebiasis hould be considered when ex

Acta paediat 44 [illegible] November 1955.

(BCG) 100 mg by mouth for three weeks. Mitsuda tests three weeks later were positive in 40.9% Fifteen were children of lepers isolated from their parents since birth. A few months to four years after the first immunization with Calmette vaccine the Mitsuda reaction was positive in 46.15% of this group Three weeks after revaccination the reaction was positive in five children previously negative, and negative in four with earlier positive or doubtful reactions. It remained the same in six.

These results are not so striking as those reported by others there is no obvious explanation since vaccine was of good quality and the method correctly employed Occasionally patients are allergic to BCG and do not react to tuberculin despite repeated vaccinations This is unexplained except that it seems related to congenital anergy Perhaps a similar phenomenon affects reaction to lepromin since results similar to these have also been reported by others. Rotberg stated that the Mitsuda test is negative in the absence of a congenital "factor N

Vaccination with BCG increases defense against leprosy and the authors propose its routine use in countries like Cuba where leprosy is endemic

Keratosis Blennorrhagica Report of Two Cases Successfully Treated with Corticotropin (ACTH) Okechukwu Ikejiani[2] (Nat'l Clinic Ibadan) describes keratosis blennorrhagica as a chronic inflammatory disease of the skin occurring with gonorrhea of the genital tract joints or eyes It is characterized by a symmetrical eruption of horny conical nodules pustules and crusts on the palms and soles and other parts of the body

Case 1—Woman, 28, complained of red eyes with a purulent discharge, joint pain hyperkeratosis of the palms and soles, and cracked lips. The Kahn test was negative but a smear of pus from the eyes and cervix revealed gonococci There was no response to large doses of penicillin, streptomycin, aureomycin • vitamins and typhoid vaccine. After use of ACTH 25 mg intravenously twice daily for two days and then 25 mg daily intramuscularly she improved immediately relapsed on discontinuance of the drug and showed prompt, complete and lasting improvement when ACTH therapy was resumed.

Case 2—Woman, 34 had complaints and lesions similar to those in Case 1 although smears and cultures of eyes and cervix showed

(2) West African M. J 4 196-203 December 1955.



Fig. 17 (top).—Silvery scaly plaques.
Fig. 18 (bottom).—[illegible] section showing numerous transected burrows and mites reduced from 35
(Courtesy of Burks, J. W. Jr., et al. A.M.A. Arch. Dermat. 74 131 140, August, 1956.)

t n of thick crusts and keratotic plaques. The more descrip- t e terms scabies crustosa and psoriasiform scabies indicate why the disease is considered in differential diagnosis f hyperkeratosis follicularis, pityriasis rubra pilaris, kera

tensive necrosis and ulceration of the skin and underlying tissues are encountered It may follow surgery or develop secondary to spontaneous external rupture of an infected organ with subsequent skin involvement The primary site is usually a colic or appendical ulceration or liver abscess. Perianal skin lesions may be found associated with amebic colitis There are also cases of cutaneous amebiasis having no direct connection with the viscera and suggesting an initial infection of the skin

Yo Seup Song[4] *(Univ of Tennessee) studied two patients* with cutaneous amebiasis for macroscopic and microscopic changes in the involved tissues and also regarding course during treatment

Man 49 was hospitalized with a sore around the anus. Three months before he had a bloody diarrhea lasting two weeks. One month later he noticed pustules around the anus which eventually drained purulent material and led to ulceration of the whole perineum. The only significant finding was a 10×10 cm. ulcer covering the entire perineum and extending through the skin, subcutaneous tissue and fascia, but not involving the muscles. The edges were indurated everted and raised above the surrounding skin. The base of the ulcer was irregular and covered with much necrotic, thick, brownish debris. Clinical diagnosis was malignant neoplasm of the rectum and a colostomy was performed.

A biopsy specimen of the perianal ulcer revealed Endameba histolytica. Beside fluid replacement therapy emetine (60 mg.) and aureomycin® (1 Gm.) were given daily for two weeks. The lesions regressed considerably with formation of granulation tissue and regeneration of skin. However the patient died 23 days after admission with diffuse peritonitis following perforation of the proximal part of the colostomy

At autopsy the perianal ulcer was covered by thick granulation tissue with apparent regeneration of skin at the edge Ulcers in various stages of development were found in the lower ileum and colon. Most were small and none extended below the superficial submucosa. Microscopic examination revealed no amebas in the perianal ulcer or in the bowel lesions, probably because of the preceding treatment.

In the second patient cutaneous amebiasis developed adjacent to the stoma of a colostomy for cervical malignancy On aureomycin® and chloroquine treatment the skin lesion healed completely

Norwegian Scabies and Norwegian itch are names given to a rare form of scabies characterized clinically by forma

(4) Am. Int. Med. 44 1211 1218, June, 1956.

Rat Mite Dermatosis Report of Small Epidemic in Dressmaking Shop is presented by K. E. Malten and R. D G. Ph Simon (Uni of Amsterdam) The workshop wa s tuated in an old building and the two worker on whom the fast moving mites were disco e ed worked in an upper room separated from the main shop in front by a stairway and a long corridor The same parasite was found among waste material in the upper hall and room. Microscop cally the parasite wa distinct from the scabies mite and identified as Lipon n bacoti H rst, a rat parasite

The plaques f dermatitis n patient A were distributed er the arms, axillae neck, thorax, back and pelvis. Th primary lesion was round o oval, 2 3 mm n diameter frequently edematous and light red. It often had a small central erosion scab or nf equently a small central hemorrhage N w lesion were sometimes double this si e with pro no nced edema and a central clear blister Lesions were clustered tog ther to produce larger plaques (to 5×13 cm) contai ng lder and fresh lesions. Between individual lesions wer m ld secondary changes cons ting of sl ght redness, pity ria s-l ke scaling hypertrophy and brownish yellow p g mentation. These skin changes persisted, in various tages, nearly 10 weeks.

Pat ent B had similar lesions and localization wh ch lasted seven week

I tient A had first worked alone in the upper room start ing when this was changed from a rag store room into a work oom Skin hanges had first ppeared when patient B joined her to work in the sam room n the latter symptoms de loped a little later After a few weeks ne girl n the front hop had skin symptoms. There was light chance that the m te themsel es had covered this considerable distance t w more l kely that the girl who carried coffee to the two w rker upstairs had provided the mi ing link She had compla d f some kin irritation, but was not examined The tw w rk r in the upper room practically never came nto th f ont shop One of tw ch ldren nd the husband of pa t ent A (who never had been n the hop) acquired symp t m eight week later Patient B li ed alone in room ther l ng in thi house were not nfected.

Although mites were found in waste sacks n the upper

Nederl. ...

toderma blennorrhagica, rupioid psoriasis and crusted erythroderma

James W Burks Jr Rodney Jung and William M. George[5] (New Orleans) observed two patients with Norwegian scabies

CASE 2.—Man 32, noted "little water blisters between the fingers. During the next three weeks the eruption spread over the body with subsequent formation of thick scaly piled up crusts over the volar surfaces of the little fingers. He complained of some nocturnal itching especially over the buttocks.

The skin was warm and slightly dry the abdomen, penis, scrotum and back as well as the flexures of the wrists, elbows and axillae were covered with many small excoriated and erythematous papular lesions. The palms and the periungual and subungual areas were covered by thick gray crusts. The feet were similarly but more severely involved so that walking was painful the nails showed secondary changes resembling onychomycosis. The elbows, upper intergluteal area and most of the lower buttocks were covered with thick, leathery firmly attached crusted plaques (Fig 57) In a small crust, S scabiei adult mites, larvae and eggs were found in large numbers. Biopsy of a crusted lesion showed many burrows and numerous transected mites (Fig 58)

Norwegian scabies appears to be an infestation with Sarcoptes scabiei var hominis (Hering) Cutaneous peculiarities hygiene basal metabolic rate estrogen effect and nutrition appear to be of little importance to the natural history of the disease. The frequency with which it is found in mongolism and in mentally defective persons is noteworthy In Norwegian scabies cutaneous sensitivity to sarcoptes antigen is found to be decreased itching is decreased, and plasma vitamin A levels are decreased Each of these may contribute to development of the hyperkeratinization seen in this rare disease Administration of vitamin A appears to be a valuable adjunct in treatment consisting of hydrogen peroxide soaks and sulfur ointment.

► [The low plasma levels of vitamin A in these two cases and the reported smoothness of the hyperkeratotic skin following administration of vitamin A are most interesting In an addendum the author stat that in a third case the vitamin A level in the plasma was normal Therefore tudy in a greater number of cases is necessary before t can be ccepted that many cases of Norwegian scabies show thi metabolic abnormality

In general it can be said that laboratory investigations for carotene and vitamin A levels, studies for night blindness, etc have been f little aid in assessing the probable clinical effects of vitamin A administration in such dermatoses as keratosis follicularis, pityriasis rubra pilaris, acne vulgaris, etc.—Eds.]

(5) A.M.A. Arch. Dermat. 74 131 140, August, 1956.

Rat Mite Dermatosis Report of Small Epidemic in Dress making Shop is presented by K. E. Malten and R. D G Ph. Simons (Uni of Amsterdam) The workshop was situated in an old building and the two workers on whom the fast moving mites were discovered worked in an upper room separated from the main shop in front by a stairway and a long corridor The same parasit was found among waste material n the upper hall and room. Microscopically the para ite was distinct from the scab es mite and identified as Lipony us bacoti Hirst a rat parasite

The plaques of dermatitis in patient A were distributed ver the arms, axillae, neck, thorax, back and pelvis. The primary lesion was round or oval 2 3 mm. in diameter fre quently edematous and light red. It often had a small central erosion, a scab or infrequently a small central hemorrhage. New lesions were sometimes double this ize, with pronounced edema and a central clear blist r Lesions were clus tered together to prod ce larger plaques (to 5×13 cm.) con t i ing older and fresh lesio s Between indi idual les ons were m ld secondary changes consisting of slight redness, pity ia is-l k scaling hypertrophy and brown sh yellow pigmentation These skin changes persisted, in arious stages, nearl 10 weeks

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(Nederl. tijdschr. geneesk. 100 142 145, Jan. 21 1956.

corridor a rat extermination campaign carried out shortly before the outbreak was the most important epidemiologic factor No new cases were reported after the workshop plant and goods had been sprayed with an insecticide containing hexachlorocyclohexane.

Extragenital Forms of Cutaneous Bilharziasis Abdel Monem El Mofty[7] (Cairo) describes three male patients, aged 11 17 who had cutaneous bilharziasis in sites remote from the natural orifices The infection was relatively recent and exclusively with hematobium The site affected was always the trunk The primary lesion was a firm ovoid papule of the same color as the skin without erythema reaching a size of



Fig 59 (Courtesy of El Mofty A. M. Brit. J Dermat. 68 252-257 July-Aug., 1956.)

2 3 mm. The papules were partly embedded in the skin and partly projected above it Later they agglomerated to form slightly raised plaques of irregular contours (Fig 59) The skin over old nodules sometimes appeared deeply pigmented scaly and abraded and later ulcerated The lesions took one to two months to develop from papules to nodules. There was no pustulation of any of the papules The lesions were always symptomless and were not accompanied by development of subcutaneous masses or infiltrations

(7) Brit. J Dermat. 68 252 257 July-Aug 1956.

The three forms of bilharziasis of the skin are, first the stage in which cercariae invade the skin second, a parasitemic phase in which the cercariae are disseminated to the tissues of the body including the skin (those reaching the portal circulation survive, the rest are destroyed) and, third the stage in which granulomas are developed in the skin near the natural orifices or in aberrant situations in response to the irritation of bilharzia ova deposited there

Any hematobium ova passing into the blood stream and reaching the general circulation are trapped by the fine arterioles of the lung. This pulmonary sieve prevents frequent arterial dissemination of the ova. However it is probable that under certain conditions in which there is obstruction of the alveolar capillaries the arteriovenous anastomotic mechanism in the pulmonary circulation is accentuated, thus allowing the ova to pass this efficient filter and to reach the systemic circulation.

"Kissing Bug" Bite. T L. Shields and E. N Walsh[8] (Fort Worth, Tex.) report their observations on 45 patients with lesions caused by the bite of Triatoma sanguisuga an insect commonly known as the "kissing bug and found principally in the southern half of the United States.

The following types of reactions were seen

1 Papular lesions with a central punctum typical of but usually severer than, ordinary insect bites. Where lesions were grouped, the diagnosis of an atypical herpes zoster was often mistakenly made. Biopsy of one of these lesions on the third day showed a nonspecific lymphocytic infiltration not identifiable as characteristic of an insect bite.

2 Grouped small vesicles in an area 2 3 cm. in diameter produced by one bite, with moderate swelling little redness and no definite central punctum. This type of reaction was most commonly seen on the arms, and in several patients a previous diagnosis of contact dermatitis had been made. The presence of other types of bite reactions in the same person helps in making the diagnosis.

3 Giant urticarial-type lesions in which a central punctum may or may not be visible. These are firm wheals 10-16 cm. across with brawny edema of a large area. In most patients the wheal was erythematous.

(8) A.M.A. Arch. Dermat. 74 14 21, July 1956.

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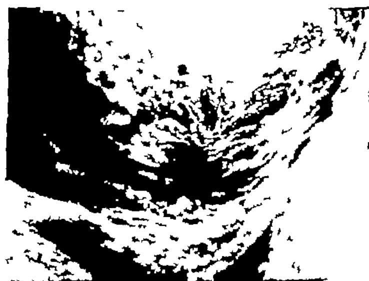


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2 3 mm. The papules were partly embedded in the skin and partly projected above it Later they agglomerated to form slightly raised *plaques of irregular contours* (Fig 59) The skin over old nodules sometimes appeared deeply *pigmented*, scaly and abraded and later ulcerated The lesions took one to two months to develop from papules to nodules There was no pustulation of any of the papules The lesions were always symptomless and were not accompanied by *development of subcutaneous masses* or infiltrations

(7) Brit. J Dermat. 68:252 257 July-Aug 1956.

The three forms of bilharziasis of the skin are, first the stage in which cercariae invade the skin second, a parasitemic phase in which the cercariae are disseminated to the tissues of the body including the skin (those reaching the portal circulation survive the rest are destroyed) and, third, the stage in which granulomas are developed in the skin near the natural orifices or in aberrant s tuations, in response to the irritation of bilharzia ova deposited there.

Any hematobium ova passing into the blood stream and reaching the general circulation are trapped by the fine arterioles of the lung This pulmonary sieve prevents frequent arterial dissemination of the ova. However it is probable that under certain conditions in which there is obstruction of the alveolar capillaries the arteriovenous anastomotic mechanism in the pulmonary circulation is accentuated, thus allowing the ova to pass this efficient filter and to reach the systemic circulation.

"Kissing Bug" Bite. T L. Shields and E. N. Walsh (Fort Worth, Tex.) report their observations on 45 patients with lesions caused by the bite of Triatoma sanguisuga an insect commonly known as the "kiss ng bug and found principally n the southern half of the United States.

The following types of reactions were seen

1 Papular lesions with a central punctum typical of, but usually severer than, ordinary insect bites. Where lesions were grouped, the diagnosis of an atypical herpes zoster was often mistakenly made. Biopsy of one of these lesions on the third day showed a nonspecific lymphocytic infiltration not dentifiable as characteristic of an insect bite.

2 Grouped small vesicles in an area 2 3 cm. in diameter prod ced by one b te with moderate swelling little redness and no definite central punctum. This type of reaction was most commonly seen on the arms and in several patients a previous diagnosis of contact dermatitis had been made. The presence of other types of bite reactions in the same person helps in making the diagnosis.

3. Giant urticarial-type lesions in which a central punctum may or may not be visible. These are firm wheals 10-16 cm across with brawny edema of a large area. In most patients the wheal was erythematous.

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(3) A.M.A. Arch. Dermat. 74:1 21 July 1956.

4 Hemorrhagic nodular to bullous lesions on the hands or feet. These are the most characteristic severe bite reactions produced by the triatoma and can be recognized as a "kissing bug" bite (Fig 60) They may be the only lesions seen or may occur with lesions of other types on other parts of the

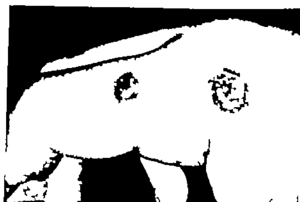


Fig 60—Typical hemorrhagic erythema-multiforme like lesions on hand (Courtesy of Shields, T L and Walsh, E N A.M.A. Arch. Dermat. 74 14 21 July 1956)

body They are multiple and suggest erythema multiforme except that they are usually unilateral

Lymphangitis and lymphadenitis may be associated with the last two types The type of reaction apparently depends on the sensitivity or allergic state of the patient toward some substance introduced at the time of the bite Patients who had had previous bites had the severest reactions. Treatment after the diagnosis is established is symptomatic

► [No lover's touch, this "kiss." And here too, allergy plays a role, not like Cupid, mind you, but with an arrow just as devastating Once sensitive all the more severe the response—yea, but t the lonely "kiss" of Triatoma sanguisuga.—Eds.]

Flea Infestation as a Cause of Papular Urticaria Preliminary Investigation. A parasitic cause for the eruption of papular urticaria in young children has been suspected for some time. Previous observers have noted the variety of the lesions, from an oval urticarial flare small solid papules vesicles bullae and crusted impetigo lesions to residual macules and small pigmented areas The eruption appears in crops of spots lasting some three days in an active irritable state followed by gradual resolution with healing of the excoriated

skin New lesions appear at intervals and the condition may last several years. Irritation is intense The eruption of papular urticaria often shows varying lesions simultaneously and it is striking that the rash does not resemble adult urticaria. Individual spots persist and go through a process of resolution which takes several days.

R. Mason Bham and E. T Burtt (Newcastle-upon Tyne) investigated 30 instances of papular urticaria at the hospital and at the homes of the patients. In 21 fleas were found or were hatched out from dust samples. Disinfestation of home and pets resulted in clearance of the eruption and kept 14 of 21 patients free It was felt that most cases of papular urticaria arise from parasitic infestation, though initially this may be obscure The problems involved are shown in the following case

Girl, 9 had had spots on the body since she was a few months old. The rug on which pet cat slept was covered with eggs, and nearly full-grown larvae were found wriggling among the materials of the rug.

► [Another piece of evidence supporting the opinion that most cases of papular urticaria are due to infestations rather than allergies or other factors This report is especially impressive since fleas were recovered from the environment in 21 of the 30 cases —Eds.]

Seabather's Eruption was observed by John S Strauss[1] (U f Pennsylvania) in about 75 persons after exposure in the area of Guantánamo Bay in Cuba. All age groups were involved Only a few persons reported itching while in the water the typical erythematous pruritic papules and welts usually appeared 12 24 hours later but occasionally not for 3-4 days In general, the lesions were follicular The characteristic site of involvement was the bathing suit area and usually the axilla Lesions were seen rarely on the neck, in the antecubital fossae and in the popliteal spaces. All lesions appeared where there was the greatest likelihood of slow drying exposed areas were free from lesions in all but about h e patients In about 50% of patients available for follow up there was a febrile response with fever up to 102-103 F nausea, malaise and some vomiting Systemic symptoms were seen in adults as well as children

White blood cell counts and sedimentation rates were normal in 13 patients differential counts were normal except

Brit. M. J. 1130 1133, May 19, 1956

(1) A.M.A. Arch. Dermat. 74 :293, September 1956.

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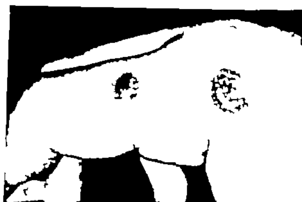


Fig 60—Typical hemorrhagic erythema-multiforme-like lesions on hand. (Courtesy of Shields, T L and Walsh, E N A.M.A. Arch. Dermat. 74 14-21, July 1956.)

body They are multiple and suggest erythema multiforme except that they are usually unilateral

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with paresis rarely react to challenge. Patients with latent, congenital, gummatous syphilis and tabes showed reaction to challenge which seems to represent reinfection or superinfection.

Intracutaneous noculation of four graded doses of virulent T pallidum (Nichols strain) into each of eight nonsyphilitic human volunteers gave a 50% infectious inoculum of pproximately 57 organisms in rabbits, it was 23 organ isms Thus, the Nichols strain of T pallidum maintained a high degree of infecti ty for man. Intracutaneous and subcuta eous injection of 50,000,000 heat-killed T pallida produced n anamnestic rise in treponemal mmobilizing test (TPI) antibodies in some subjects previously treated for syphilis, but failed to ncrease reagin t ters significantly No hanges n circulati g antibodies were demonstrated n nonsyphilitic controls given this antigen

F fty fou previously syphil tic volunteers were noculated intracutaneously at a single site with 100,000 virulent T pal lida All but fi e had presumably had adeq ate treatment for their earlier infection The five with untreated latent syphilis showed no clinical or serologic response to challenge and were presumed resistant to superinfection Of 11 subjects previously treated f r presumed or proved early syphilis, 9 dev loped darkfield pos tive lesions and 2 developed darkfield-negative lesions. All showed increased serologic tests for syphilis (STS) titers and were considered t have been fected by the virulent inoculation. Reagin developed and TPI titer increased much more rapidly than in non syphilitic controls. Of three subject prev ously treated for proved or presumed reinfection one developed a darkfield-positive lesion, another darkfield-negat e les on, both w th increased STS t ters e had no clinical or serologic re sponse to challenge Of 26 subjects pre iously treated for proved presumed late latent syphilis 10 were considered fected One developed a darkfield-posit e lesion nine showed darkfield-negati e lesions, one a gumma, all with creased STS titers. Darkfield-negat ve lesions not associ ted with STS titer increases de eloped in 3 subjects and 13 h wed no clin cal or serologic change. Among five subjects t eated for proved o presumed congenital syphilis darkfield-positive lesion developed in one nd darkfield

for relative eosinophilia (4-7%) in 4 Stool examinations were done on 48 patients two weeks and on 17 patients five weeks *after appearance of the dermatitis* Direct smears and alcohol sedimentation tests were negative for parasites in all but one patient who had endameba *trophozoites. Complement fixa*tion tests for schistosomiasis were negative

In contrast to seabathers eruption for which the etiologic agent has not been identified, swimmers itch has definitely been shown to be a sensitivity phenomenon involving avian schistosomes. *In swimmers* itch the exposed areas of the body are involved whereas in seabathers dermatitis most involvement is *of the covered areas Apparently these are* two distinct clinical entities

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8 VENEREAL DISEASES AND THEIR TREATMENT (EXCLUSIVE OF GONORRHEA)

Inoculation Syphilis in Human Volunteers is reported by *Harold J Magnuson* Evan W Thomas Sidney Olansky Bernard I Kaplan Lopo De Mello and John C Cutler[2] in a *study in which 62 volunteers at Sing Sing Prison* were inoculated with virulent Treponema pallidum

Literature on human inoculations with syphilis reveals the following facts The nonsyphilitic is highly susceptible to infection with T pallidum *if it is* introduced into or below the skin. *Rabbit* and anthropoid passed strains of T pallidum retain their infectivity for man The *local lesion* on genital mucous *membrane differs from* that found on the skin A state refractory to challenge as the duration of the untreated disease increases seems to depend on size of the inoculum, method of inoculation and unknown host factors The lesion of challenge tends to conform to the stage of syphilis reached by the original infection but with *numerous exceptions.* Nodules and gummatous lesions most commonly followed challenge in persons with previous late syphilis Reaction of the person previously exposed to syphilis differs from that of the previously nonsyphilitic The progressive reactions result from living T pallidum and not from tissue proteins or heat killed T pallidum. There is incontrovertible proof of superinfection in persons with gummatous lesions Patients

(2) Medicine 35 33-82, February 1956.

of whom had had no previous treatment. The observation period of groups large enough to perm t alid findings extended through six to seven years. The amount of penicillin administered as study treatment aried from less than 2,400,000 units given to 4 4% of patients, to 9,000,000 or more received by 40% The maximal cumulati e probability of progression to sympt matic neurosyphili after penicillin therapy i 0.55% the first year 1 69% the third year 2.02% the fifth year and 3 31% the seventh year after treatment.

Only 12 patients of the 765 treated showed progres ion of asymptomatic neurosyphilis at the last observation period. Only one of them was unequivocally classified as having treatment failure this patient responded sati factorily to treatment w th larger dose of pen cillin In the other there was no learcut evidence that the so-called progres ion represented progress of the disease

In this group progression could not be related to any factors considered in the analysis, except in a single patient in whom lack f co-operation precluded administration of treatment when cerebrospinal fluid exam nation clearly indicated relapse requiring treatment. Progression, with one exception, consisted of minor neurologic o psychiatric changes non of the patients was incapacitated by it.

Progression probably represents man festation at the level f clinical recognition of pre-existing subclinical neuraxis damage. A ymptomatic central nervous system syph lis responds extremely well to treatment with penicillin It is felt that penicill alon is capabl of completely curing it.

II Results of therapy as measured by laboratory find ngs were also evaluated by the Co-operative Cl nical Group in the 765 patients with asymptomatic neurosyphilis. Results nd cated that th range of cell count of 5-10 and total protein f 40-50 mg /100 cc. is borderline and probably with n normal l m ts. After successful treatment, abnormal cell counts d sappear almost completely w thin four years total protei alues change mor slowly but do not show the same degree of reversion to what s considered normal limits within that period.

A measured by fall cell count, the most sen tiv ndex, n learcut relation between treatment success or failure

( ) A.M.A. Arch. Dermat. 74:347-377 October 1956.

negative lesions one a *gumma* associated with increase in serologic titer in three. One showed no clinical or serologic evidence of infection Of two persons previously treated for asymptomatic central nervous system syphilis one may have developed such a reinfection the other showed no evidence of reinfection Subjects who had previously had syphilis differed from nonsyphilitic controls in their reaction to infection In general this was influenced by duration of the original infection before treatment but there was much individual variation There is some evidence that administration of heat killed T pallidum may have produced a booster effect in the immunity of patients previously treated for syphilis but other variables make further confirmation necessary

These experiments represent the first published quantitative measurement of the infectiousnss of T pallidum for man It was possible to determine the 50% infectious inoculum for the normal person It is emphasized that patients who have once had syphilis although cured in the primary stage are immunologically never the same, as shown by accelerated response in both the lipid antigen and the TPI tests Types of serologic response are like those observed in anamnestic rises to other antigenic stimuli Development of gummatous lesions in two of the previously well treated subjects demonstrates that the particular type of allergy productive of gummas may persist for years Completion of an experiment of this nature without untoward incident suggests the feasibility of further human studies The course of syphilis illustrates many of the problems of chronic infectious diseases and the availability of safe effective therapy permits direct experimental approach to some of the broad immunologic problems which cannot be as readily studied in diseases for which such treatment is lacking

► [A fascinating study which answers some of the many important questions regarding syphilis about which there has been much speculation in the past. Among the most impressive results is that, no matter how complete the cure a patient who has once been infected with T pallidum immunologically does not return to his original state —Eds.]

Penicillin **Treatment of Asymptomatic Central Nervous System Syphilis**—*I Probability of progression to symptomatic neurosyphilis* was studied by the Co-operative Clinical Group[3] (U.S P H S Washington D C) in 765 patients 264

(3) A.M.A. Arch Dermat. 74 355-366, October 1956.

used throughout. The base line for this group was that it was a representative sample of untreated seropositive syphilis in the male Negro. Duration of syphilis in the patients varied from a few months to 72 years. There was clinical evidence of aortitis in 23.6% of central nervous system involvement in 7.8% and of bone, joint and skin involvement in 11.5%.

In untreated syphilis, the percentage of serologic reversal to negative by the Kahn test was lowest in patients aged 25-39 with syphilis of less than 15 years duration, highest in patients aged 55-69 with syphilis of 30-44 years duration. A small amount of treatment (3-20 arsenical injections) administered to the former increased the seronegativity rate but did not influence it in the latter group. It was estimated that less than 50% of untreated syphilis will be detected 30 years after infection. In untreated syphilis the treponemal immobilizing test did not appear to become nonreactive with time. Clinical manifestations of late syphilis were seen in 27% of patients with spontaneous serologic reversal. The pattern of seroreversal in untreated syphilis was as variable as treated syphilis.

Prevention of Congenital Syphilis by Treatment of Syphilis in Pregnancy. Nels A. Nelson and Virginia R. Struble[a] (City Health Dept. Baltimore) found that in 1,220 children of 423 mothers with histories of infection with syphilis the incidence of congenital infections in children of untreated mothers was 13.4%. In children of inadequately treated mothers it was 5.8%. No congenital infections occurred among children of mothers who had received at least one full course of antisyphilitic therapy whether with arsenicals, bismuth or penicillin. A course was defined as the amount of treatment held to be desirable at the time the mother was treated and given within a reasonable period without excessive delinquency. For mothers treated with an arsenical and heavy metal, this varied from an intensive course of 30 injections of an arsenical (usually oxophenarsine hydrochloride) and 10 injections of bismuth subsalicylate in 10 weeks to alternating courses of 8 weekly injections of an arsenical (usually neoarsphenamine) and 8 weekly injections of bismuth subsalicylate to a total of 64 injections. If the patient treated by the latter schedule received 20 injections of each drug it was

[a] J.A.M.A. 161:869-872, June 30, 1956.

and size of penicillin dosage could be demonstrated. It appears that persistently abnormal cerebrospinal fluid total protein levels are not indicative of poor prognosis

Significant differences in total protein response were observed in relation to sex and race. The outcome was less favorable in white persons than in Negroes and in males than in females

Cerebrospinal fluid tests for syphilis showed a gradual decrease in positivity with passage of time after treatment this was more pronounced in the group receiving only a single course of penicillin

Improvement in cerebrospinal fluid test for syphilis is more rapid in the younger patient in one with disease of shorter duration or in one with abnormal cell count A minimum of 28% of the patients with asymptomatic central nervous system syphilis had a blood serologic titer of 2 units or less. Thus a weak serologic reaction cannot be considered indicative of absence of cerebrospinal fluid involvement. After penicillin treatment for asymptomatic central nervous system syphilis there is a gradual trend toward seroreversal

There seemed to be no relationship between serologic negativity and degree of cerebrospinal fluid positivity at onset of study treatment

Changes in the blood serologic test for syphilis following penicillin treatment do not reflect with any degree of accuracy changes in the cerebrospinal fluid test for syphilis.

Asymptomatic central nervous system syphilis responds extremely well to treatment with penicillin Retreatment on the basis of persistent positive laboratory findings alone is not recommended unless the cell count increases significantly after treatment remains unchanged at an elevated level for six months or increases significantly after approaching normal or near normal level after treatment

► [These results in a large and well studied series attest once more to the excellent effects of treatment with penicillin alone in asymptomatic central nervous system syphilis.—Eds.]

Untreated Syphilis in the Male Negro Twenty two Years of Serologic Observation in a Selected Syphilis Study Group Sidney Olansky Ad Harris, John C Cutler and Eleanor V Price[5] (U.S P H S Washington D C) report on a group of 431 syphilitic men followed since 1932 The Kahn test was

(5) A.M.A. Arch. Dermat. 73 516-522, May 1956.

able effect of the hormone on this reaction is ascribed to the same mechanism by which it inhibits hypersensitiveness and symptoms of many infections during the course of which an allergy-immunity state develops. Concurrent administration of penicillin and prednisone to patients with syphilis makes it possible to prevent in many cases undesired consequences that may follow Herxheimer's reaction.

► [These results confirm those reported by de Graciansky and Grupper (Semaine hôp Paris 31 1, 1955) —Eds.]

Significance of Treponema Pallidum Immobilization Test on Spinal Fluid is discussed by J Lowry Miller, Meyer H Slatkin and Justina H Hill (Columbia Univ.) There were 376 specimens of spinal fluid from 324 patients on which the standard serologic tests for syphilis (STS) and the T pallidum immobilization (TPI) tests were performed, in addition to standard tests on all specimens of blood from 293 patients. The immobilization test was done by the method of Magnuson and Thompson with 22.2% complement results were interpreted by the method of Nelson and Mayer.

In 46 patients with asymptomatic neurosyphilis, the spinal fluid TPI tests gave positive results in 6 patients when the STS was negative, both test reactions being positive in the blood. In five patients, the TPI results in the spinal fluid were negative, whereas in the STS and in both tests on the blood, they were positive. All five patients had received large amounts of penicillin previously. Thus, negative TPI results on the spinal fluid may erroneously exclude neurosyphilis.

Studies to date confirm the validity of the results of the TPI test on the blood, barring laboratory error and exclusion of other treponematoses. However, in 54 patients with tabes dorsalis, paresis, meningovascular syphilis and primary optic atrophy in whom the diagnosis could be established on clinical grounds, the immobilization test on the spinal fluid showed negative results in 8. The STS reaction in the spinal fluid in the same group was negative in nine patients. On spinal fluid tests of these 54 patients, there were 13 discrepancies between the clinical diagnosis and the TPI and STS. The TPI alone was negative in four, the STS alone negative in five and both negative in an additional four. In a series of 100 patients with a diagnosis of neurosyphilis there

(1) J.A.M.A. 160:1294-1297, Apr. 21, 1956.

considered that she had had a course of treatment, even though she did not receive the entire 64 doses A course of penicillin treatment might consist of 1,200,000 or 2 400,000 units of soluble penicillin combined with a few doses of an arsenical and bismuth usually given in a hospital or 4,800, 000 units or more of procaine penicillin in a form that maintained significant blood levels for several days usually given on an ambulatory basis

If a pregnant woman has received at least one full course of treatment without relapse or a reinfection since, there is little or no risk of infection in her children although her serologic tests may be positive even at high titer If however the mother s tests are positive, the infant s tests may also be positive up to several weeks due to transfer of the mother s reagin to the fetal circulation Lacking clinical evidence it may be impossible to establish diagnosis of infection in the child until it is at least 3 months old It does not matter how long before delivery or pregnancy treatment is given Retreatment during subsequent pregnancies is unnecessary unless there has been relapse or reinfection or a possibility of these

Influence of Prednisone on Herxheimer s Reaction in Syphilis was tested by Modesto Depaoli[7] (Univ of Turin) in eight patients with primary syphiloma of at least 15 days duration and in nine with secondary syphilis. All received one injection of 300 000 units of penicillin in aqueous solution one hour at least after the first dose of prednisone This was given orally every 4 or 5 hours to a total dose of 15-25 mg in 12 or 24 hours At the same time 10 controls with primary syphiloma and three with secondary syphilis were given 300 000 units of penicillin only

Temperature rose markedly in all the controls within four to six hours and clinical manifestations became accentuated in those with secondary syphilis Herxheimer s reaction was completely inhibited in seven patients with chancre and four with secondary syphilis markedly attenuated in one with chancre and one with papular syphilis appeared only after 14 hours in one with secondary syphilis and was not influenced in three with papular syphilis two of whom had not been given a sufficient amount of prednisone The favor

(7) Minerva dermat. 31:263-267 September 1956.

abl effect of the hormone on this reaction is ascribed to the same mechanism by which it inhibits hypersensiti eness and symptoms of many infections during the course of which an allergy immunity state develops. Concurrent administration of penicillin and prednisone to patients with syph lis makes it possible to prevent in many cases undesired consequences that may follow Herxheimer s reaction.

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(9) J A M A 160:1394 1397 Apr 21, 1956

was a discrepancy in the TPI of 14% compared with the clinical diagnosis and of 16% in the STS compared with the clinical diagnosis

A positive TPI reaction of the spinal fluid is diagnostic of neurosyphilis The negative results of spinal fluid TPI tests are probably related to low amounts of immobilizing antibody present Reversal of spinal fluid specimens after freezer storage from positive to negative immobilization reactions may be due to initial low antibody level and subsequent fall of antibody as a result of storage. It is recommended that spinal fluid TPI tests be done immediately to prevent this decrease in antibody It is concluded that positive immobilization test results in spinal fluid are diagnostic of neurosyphilis *but negative results may not* exclude the diagnosis.

Treponema Pallidum Complement Fixation Test (TPCF) is compared with tests using lipid antigens, serologic tests for syphilis (STS) and the treponemal immobilizing test (TPI) by Harold J Magnuson and Joseph Portnoy[9] (U S P H S Washington, D C) The TPCF test uses virulent Treponema pallidum, obtained from infected rabbit testes and then concentrated The lipid fraction is removed by successive acetone and ether extractions and the active protein like antigen is removed in 0.2% sodium desoxycholate solution The resultant antigen is used in the conventional complement fixation test similar to the fifth volume Kolmer technic.

In 395 patients with treated and untreated syphilis, the *TPCF test seemed more reactive than the TPI in primary* and secondary syphilis. In central nervous system syphilis the TPI test was more reactive Agreement of TPCF and TPI results was 87 3% The earlier appearance of TPCF antibody and reagin compared to the TPI was better demonstrated in the rabbit. Where differential diagnosis lay between biologic false positive STS and latent syphilis in 266 patients, the STS TPCF and TPI results agreed in only 33.5% although the TPCF and TPI tests agreed in 94% In 292 untreated patients the TPCF results paralleled the STS Neither the TPCF nor the TPI tests measure reagin. Therefore, the early correlation between STS and TPCF tests is

(9) Am. J Pub. Health 46 190-194 February 1956.

not due to reagin cross-activity In 379 treated patients the correlation between TPCF and TPI tests was somewhat greater than between treponemal tests and STS The new tests clearly indicate that syphilis evokes a variety of antibodies. TPCF results are as helpful as those of any other single test, but there is still no single definitive procedure.

Experimental and Serologic Investigations on Differentiation between Cultured Treponemas (Reiter) and Virulent Treponema Pallidum are reported by Kurt Meinicke[1] (Univ of Munich) Henrici stated that two micro-organisms may be considered to belong to the same genus when they show analogies (1) morphologically (2) biochemically (3) in cultivability on the same culture medium (4) in animal pathogenicity and (5) in serologic reactions.

1 Culture spirochetes (Reiter) which in animals can hardly be distinguished from virulent T pallidum, show a markedly different motility rotatory and bending movements particularly the characteristic pre-formed rigidity of spirals which persists even during most lively movements of T pallidum, were not observed.

2 Biochemical differences between culture spirochetes and virulent T pallida have been reported by other investigators

3 Culture experiments revealed that culture spirochetes grow easily on liver in liver-bouillon nutrient medium whereas T pallidum could not be cultured on artificial nutrient mediums. As far as growth on such mediums is concerned, culture spirochetes rather show marked analogies with the saprophytic genital spirochetes T calligyrum and T genitalis.

4 Animal pathogenicity is also different in T pallidum and in culture spirochetes. Animal experiments showed that intratesticular injection of culture spirochetes never produced a syphilitic infection in rabbits. Culture spirochetes are therefore apathogenic.

5 In a further series of animal experiments it was found that after intratesticular injection of living culture spirochetes, antibodies against culture spirochetes were formed, but not specific antibodies which immobilize virulent T pallida. When rabbits were infected with virulent T pallidum, lipoid reagins antibodies against culture spirochetes and

(1) Hautarzt 7:433-437, October, 1956.

specific T pallidum immobilizing antibodies formed. After rabbits were immunized by suspensions of dead culture spirochetes antibodies against the antigen used could be demonstrated in the serum of the animal up to a titer of 1:640 Specific antibodies were not formed Immunization with dead T pallida elicited in vivo the formation of specific antibodies up to a titer of 1 1280 Lipoid *reagins* and *protein* antibodies against culture spirochetes were also produced Serums of untreated patients (secondary and latent syphilis) with positive Nelson tests did not immobilize culture spirochetes

Culture spirochetes (Reiter) and virulent T pallida differ in *all* five criteria Therefore, apathogenic, saprophytic culture spirochetes do not belong to the genus T pallidum. Results of these experiments and serologic investigations prove that culture spirochetes and T pallidum can clearly be distinguished serologically from one another and that the antigen structure of culture spirochetes is different from that of virulent treponemes (T pallidum pertenue and cuniculi)

VDRL Chancroid Studies IV Experimental Chancroid, Prophylaxis and Treatment. Wilbur E. Deacon Sidney Olansky David C *Albritton and William Kaplan*[2] (*U.S P H.S* Chamblee Ga.) conducted two experiments in human volunteers One dealt with the ability of certain antibiotics combined in commercial ointments and cream to prevent Hemophilus ducreyi infections when applied topically to previously inoculated skin sites *In* the other experiment the possible usefulness of penicillin orally as a prophylactic and therapeutic agent was investigated.

Results of the first experiment indicate that erythromycin and chloramphenicol are effective prophylactic agents for H ducreyi infections. The dramatic results obtained with chloramphenicol prophylactically and therapeutically suggest its use in treatment trials The second experiment showed that prophylaxis occurs with penicillin V when adequate serum levels were established before inoculation with virulent H ducreyi

(2) Antibiotic Med. 2 141 147 March, 1956.

Experimental Investigations on Pathogenesis of Contact Dermatitis. J. R. Frey and P. Wenk[1] (Basel) studied the place and time of pathogenic changes in experimental dinitrochlorobenzene (DNCB) dermatitis of guinea pigs, followed up the various stages from the first contact with DNCB to the appearance of generalized sensitization and attempted to distinguish the various participating organs and tissues.

METHOD.—White guinea pigs of either sex and weighing about 500 Gm. were used. The primary toxic lesions were produced after electric shaving by application of solutions of DNCB in acetone (5% to areas of 4 sq. cm., 10% to areas 3 mm. in diameter) or simply by using a small DNCB crystal. The lesions were covered with double adhesive tape and gauze pad. Changes in cutaneous reactivity were tested after 8-10 days by application of 0.025 ml. of 0.3, 0.5 and 0.9% solution of DNCB in acetone to orbicular areas of 2 sq. cm. For controls, in most experiment groups of four previously sensitized animals with positive reactions (positive controls) and four guinea pigs without previous contact with DNCB (negative controls) were used. Anesthesia was produced with an ether-air mixture, and scissors were used for excisions.

The application of concentrated solution of DNCB to small skin areas (primary contact) of guinea pigs was followed within a few hours in all animals by simple changes common to DNCB (primary toxic reaction). When nine days later DNCB was again applied (secondary contact) the same animals exhibited characteristic inflammatory changes (test reaction) even after application of concentrations which normal animals tolerated without a reaction. Owing to primary contact the reactivity of the entire skin has changed, and animals become sensitized after a certain time (incubation period). The minimal contact time in which DNCB produces cutaneous sensitization in guinea pigs is 32 hours; the incubation period, i.e., time between primary contact and sensitization of the whole skin, is 6-9 days. Compared with incubation period, minimal contact time is relatively short. This presumably indicates that during this phase of contact dermatitis the skin serves only as the port of entry and that important changes are taking place in other parts of the body.

(1) Dermatologica 112 : 265-305, Apr.-June, 1956.

The manner in which test reactions originated from the area of contact was studied by aid of skin explants. Skin areas in one group of animals were connected with the rest of the body by arteries veins and nerves only and in another group also by a cutaneous bridge. In 44 animals of the first group DNCB was applied to the skin explant, but sensitization did not occur either in the normal skin or in the explant. When DNCB was applied to normal skin in 17 animals of the same group the test reaction was positive in the skin explant. It can be concluded that skin explants remain viable and that *effects arising from* the area of contact are transmitted not by the circulatory or nervous system but by lymph vessels to regional lymph nodes. This seems evident by the fact that in 32 animals DNCB applied to the skin explant with vascular connection and a cutaneous bridge (containing also lymph vessels) produced sensitization. Regional lymph nodes of the contact site proved to be essential for sensitization When regional lymph nodes of the contact site were removed before primary contact sensitization did not occur despite an existing connection through blood vessels nerves and skin. It is assumed that with essential parts of the skin DNCB may form full antigens which possess sensitizing capacities and are transported into lymph nodes The importance of lymph nodes lymphatic organs lymphocytes and leukocytes has been confirmed by experiments on passive transfer of eczematous hypersensitivity Successful results were obtained in some cases with suspensions of leukocytes lymphocytes or lymphatic organs

Vascularized skin explants became sensitized after primary contact on normal skin This result suggests that the effects which change the reactivity of the entire skin are generalized via the blood stream an assumption which is supported by the fact that lymph finally is emptied into the blood At present it seems less probable that sensitization is generalized by cerebrospinal or vegetative pathways in these vascular connections

To determine primary toxic and allergic thresholds a special quantitative method of epicutaneous testing was worked out.

METHOD.—To determine the primary toxic threshold, 1 1.5 2 and 3% solutions of DNCB in acetone were applied on the same

day to four different areas of 4 sq. cm. in eight guinea pigs. Reactions were read 24 hours later. The same experiment was repeated on the other flank after 24 hours. To determine allergic thresholds, 0.3-0.5 and 0.9% solutions of DNCB were used.

The primary toxic threshold was between 1 and 3% About 50% of all animals reacted to 2% and about 10% to 1% The allergic threshold was between 0 1 and 1% i.e approximately a tenth of the primary toxic threshold About 50% of all sensitized animals reacted to 0.5% about 5-20% to 0 3% solutions.

► [This work confirms the classic observation regarding reaction time, incubation period, etc., in allergic contact sensitization. In addition, it presents highly interesting new data, especially with respect to the role of the lymphatic pathways between skin and lymph nodes and to the local lymph nodes themselves. The technic of Frey and Wenk probably could lend itself very well also to investigation of the role of the nervous system in allergic contact sensitization. Does allergic contact sensitization take place in explants with intact blood vessels and lymph pathways but with cut nerves —Eds.]

Factors Influencing Skin Reactions in Guinea Pigs Sensitized with 2,4-Dinitrochlorobenzene (DNCB) were studied by Ake Nilzen and Kjell Wikstrom (Karolinska Hosp Stockholm) particularly with reference to administration of cortisone or hydrocortisone and to exposure to damp or dry cold.

PROCEDURE.—Male guinea pigs, sensitized to DNCB were subsequently challenged with 0 25% 0.1% and 0.05% alcoholic solutions of DNCB and 1% 0.5% and 0 25% solutions of DNCB in peanut oil One group of animals received cortisone, 20 mg /kg body weight Another group was exposed to damp cold, 50-80% humidity and 0-10 C for six hours after testing Another group was exposed to dry cold, 37 50% humidity and 5 C, for six hours after testing

There was no appreciable difference in the reactions of the group treated with cortisone and the control group although there was longer latency in the cortisone-treated group Controls responded to weaker antigen solutions Development of epidermal reaction was delayed by exposure to both damp and dry cold. Quantitative determination of epidermal reaction were not possible and slight variations difficult to appraise.

Experimental Studies on Hypersensitivity to 2,4-Dinitrochlorobenzene and Tuberculin in Animals.—III *Parabiosis Experiments*—Erik Skog[1] (Karolinska Inst., Stockholm)

[1] Acta dermat.-venereol. 35 13-419 1955. Ibid. pp. 264-276.

shows that sensitivity to 2 4-dinitrochlorobenzene (DNCB) passes to a normal parabiont both in celioanastomosis and in cutaneous parabiosis as does tuberculin sensitivity

METHOD.—White female guinea pigs 300-400 Gm., were tested with 1% DNCB in olive oil and with 1 mg tuberculin in a 1 100 dilution In celioanastomosis, the animals were united by skin, muscle and peritoneum in cutaneous parabiosis, they were joined by the skin alone for about 10 cm. With the first technic in six pairs, one of each pair was DNCB sensitive in each of another six pairs, one was tuberculin sensitive. Repeated tests with DNCB were avoided to prevent active sensitization. About 40 experiments were conducted with DNCB sensitive donor animals in which cutaneous parabiosis had been established. In these the partners were separated and tests were conducted thereafter

In the celioanastomosis group DNCB sensitivity was passed to all partners three reacting as strongly as the donor In the tuberculin group after five or six days some recipient animals reacted as strongly as the donors In the cutaneous group the DNCB sensitivity became established only after at least four days of parabiosis and it virtually disappeared in one to four days after separation of the animals in 14 of 20 experiments the tuberculin sensitivity subsided in one to five days. *In six cases the passive DNCB sensitivity remained* unchanged or increased in intensity during the experiment probably from active sensitization Except for these six the duration of passive sensitivity to DNCB and to tuberculin did not differ

II Intracutaneous passive transfer of sensitivity to 2 4-dinitrochlorobenzene and tuberculin —Skog[6] presents results of experiments with local passive transfer of sensitivity i e. with cells injected intracutaneously instead of intraperitoneally as in previous experiments Guinea pigs were sensitized and tested with a drop of dinitrochlorobenzene (DNCB) in oil and by intracutaneous injection of 0 005 mg DNCB in 0 1 cc. alcohol saline solution Tuberculin sensitivity was produced in rabbits and testing was by intracutaneous *injection of 1 mg* tuberculin in 1 100 dilution. Only strongly sensitized animals were used as donors Intracutaneous transfer of DNCB sensitivity was made with cells from peritoneal exudate spleen thymus and lymph This was also done with guinea pigs in transfer of tuberculin sensitivity When rabbits were used *only lymph was transferred.*

(6) Acta dermat.-venereol. 35 401-414 1955.

Twent three experiments were conducted, using 44 donor animals and 84 recipients.

Local transfer of tuberculin sensitivity succeeded with cells from lymph, thymus, spleen and peritoneal exudate. Similar experiment with DNCB sens tivity failed. Transfer of tuberculin sensitivity required large numbers of cell ex ceeding 3×10^{8} in experiments with rabbit lymph and ex ceeding $3\text{-}6\times10^{8}$ in those with other types of cells from guinea pigs. After five days, passi e tuberculin sensitivity was not demonstrable n recipient animals. DNCB sen tivity cannot be passively transferred by local injection of cells, but tuberculin sens tivity ca

Passive transfer experiments w th lysed cells.—Skog[1] compared transfer of lysed and untreated cells in tuberculin and 2,4-dinitrochlorobenzene (DNCB) sensit vity Guinea pigs and rabb ts were sensitized to DNCB and to tuberculin by m thod described elsewhere. Transfer was effected intra peritoneally and intracutaneously Lysed nd untreated cells were used and c ll counts made in all instances control ex periments were performed.

It was not possible t demonstrate transfer of DNCB and t berculin sensitivity with suspensions f lysed cells, although such transfer was effected with untreated cells There f re undamaged cells seem necessary to produce antibodies f r pass sensitization. Intracutaneous transfer of DNCB sensitiv ty could not be accomplished with untreated or lysed cell In sim la reported experiments (Weslen) on rabbits with bacterial ccines, ant body form ng power disappeared f lysed cells were used.

[The results of these studies fit in with evidence obtained through other experimental approaches hich show that contact sensitivity in guinea pigs can be passively transferred and that such passively acquired sensitivity is of very short duration Where sensitivity acquired during parabiosis, increased after separation of the animals, it appears likely that activ sensitization had taken place, phenomenon hich previously has been observed in animals by M W Chase and others and in man by Sulzberger and the senior editor (J Invest. Dermat. 18 53, 1952) These authors suggested that the hite cells of allergic animal and human beings contain factor hich facilitates or stimulates specific active sensitization to the homologous allergen in animals or human beings injected ith such cells

Obviously it is important that clear distinction be made between (1) passive transfer of sensitivity (here the sensitivity may be expected to last only relatively short time) and (2) passive transfer of factor

1) Acta dermat.-venereol. 34 1 10 1954.

antibodies of protein character is markedly raised and that nucleic acids are increased in organs in which protein synthesis is taking place For this reason in a third series of experiment ribonucleic acid and desoxyribonucleic acid were estimated in the kin liver and spleen of white guinea pi before and after sensitization to DNCB It was found that during ensitization of guinea pigs ribonucleic acid values in the kin were on the average 80% and in the liver 3 higher than in control animals Changes of ribonucleic ... pleen and of desoxyribonucleic acid in all exam... of en itized and of nonsensitized animals were ... These results seem to support the finding of ... of lymphocytes in the skin and their in... ...tion of antibodies in the liver

... study demonstrating changes in the circulating white ... guinea pigs during the incubation period of sensitization ... venereol. 33 359 1953) carried out blood counts ... had already been sensitized to DNCB and found an ... five to seven hours after application of DNCB ... are of course not in contradiction to those ... pertain to the period of development of sensiti...

... is the very marked increase in ribonucleic ... in the liver during sensitization, but a ... the meaning of these findings is not yet

... Sulfate on Sensitization of Guinea Pigs ... was studied by Ake Nilzen and Kjell ... Stockholm) Five groups of ... treated daily for eight days with ... potassium dichromate nickel sul... latter two combined with lauryl ... into a 6×6 cm area for two ... drop of the respective solutions ... treated skin ... treatment or testing with 1% ... aqueous potassium dichromate ... With a mixture of 1% lauryl ... chromate, treatment and test ... and infiltration With a mix... nickel sulfate one animal ... tration on both procedures ... number of animals re...

sponded to testing with potassium dichromate and nickel sulfate alone, and in the same manner as with the mixture. Biopsy specimens of skin taken after eight days from treated tes showed no changes in the first three groups but showed typ cal eczematous inflammatory reaction where the mixed hemicals had been used. Test ite biopsy speci mens from the mixed chemical groups were similar showing epidermal thicken ng intra and extracellular edema, blood essel dilation and increase of leukocytes in the upper der mis. Lauryl sulfate seemed to activate the eczematogenic properties of a simple chemical compound in guinea pigs probably by increasing skin permeability and formation of a complete antigen.

► [E idence such as this may very well be applicable to man. Perhaps the high incidence of hand eczemas now blamed on certain detergents i not the result of their direct action alone, but of increased penetration of the allergen or of local changes produced by the detergent (e.g., acanthosis) permitting greater reactivity to eczematogenic allergens and primary irritants.

The histologic findings of spongiosis and incipient vesiculation in the skin of guinea pigs (which normally does not react in such manner) after application of sodium lauryl sulfate is in consonance with our own findings (J. Invest. Dermat. 27:249 1956) —Eds.]

Delayed Allergic Skin Responses of Contact Dermatitis Type are described by Herman N. F sen[2] (New York Uni Post-Grad Med School and Skin and Cancer Unit) Animals sensitized with 2,4-dinitrofluorobenzene, after suitable incu bation, were skin tested with ten 2 4-dinitrobenzenes differ ing only in the group substituted on carbon 1 There wer si elicitors and four nonel citors of inflammatory response Th licitors combined chemically with proteins in vo and in vitro nonelicitors did not. Group I elicitors, F Br and Cl-substitutes eacted in vivo with the NH_2 groups of ly si e side hains of epidermal protein whereas group II el citors SO_3-SCl- and SCN substitutes reacted only with S of cystine or cysteine residues of epidermal protein. Group I licitors acted over a broad pH range (7.0-11 0) with a ariety of proteins in vitro but group II reacted only with hair or epidermal strips at pH 7.0-8.0.

The dinitrophenyl-protein conjugates f rmed in the living sk n were found by radioautography to be localized in the epidermis for 48 hours Thereafter the conjugates were con fi ed to the strat m corneum, gradually becoming more su-

(1) Bull New York Acad. Med. 32 239 243, March, 1956.

antibodies of protein character is markedly raised and that nucleic acids are increased in organs in which protein synthesis is taking place. For this reason in a third series of experiments ribonucleic acid and desoxyribonucleic acid were estimated in the skin, liver and spleen of white guinea pigs before and after sensitization to DNCB. It was found that during sensitization of guinea pigs ribonucleic acid values in the skin were on the average 80% and in the liver 26% higher than in control animals. Changes of ribonucleic acid in the spleen and of desoxyribonucleic acid in all examined organs of sensitized and of nonsensitized animals were insignificant. These results seem to support the findings of increased numbers of lymphocytes in the skin and their intensified production of antibodies in the liver.

► [An excellent study demonstrating changes in the circulating white-cell picture in guinea pigs during the incubation period of sensitization. Seeberg (Acta dermat. venereol. 33:359, 1953) carried out blood counts in guinea pigs which had already been sensitized to DNCB and found an increase in granulocytes five to seven hours after application of DNCB to the skin. His observations are of course not in contradiction to those of Polák whose findings pertain to the period of development of sensitization.

Of particular interest also is the very marked increase in ribonucleic acid values in skin and less so in the liver during sensitization, but a satisfactory explanation as to the meaning of these findings is not yet available.—Eds.]

Influence of Lauryl Sulfate on Sensitization of Guinea Pigs to Chrome and Nickel *was studied by Åke Nilzén and Kjell* Wikström[1] (Karolinska Hosp., Stockholm). Five groups of five animals each were treated daily for eight days with solutions of lauryl sulfate, potassium dichromate, nickel sulfate and each one of the latter two combined with lauryl sulfate. 4 drops was rubbed into a 6×6 cm. area for two minutes. After 12 days 1 test drop of the respective solutions was placed on previously untreated skin.

There was no response to treatment or testing with 1% aqueous lauryl sulfate, 0.5% aqueous potassium dichromate or 4% aqueous nickel sulfate. With a mixture of 1% lauryl sulfate and 0.5% potassium dichromate treatment and testing produced scaling, erythema and infiltration. With a mixture of 1% lauryl sulfate and 4% nickel sulfate one animal showed marked scaling and infiltration on both procedures. In the last two groups the same number of animals re-

(1) Acta dermat.-venereol. 35:292-299, 1955.

not intraperitoneal application. However when intraperitoneal administration of picryl chloride was combined with Freund's adjuvant, a water-in-oil emulsion in which killed mycobacteria are suspended, many more and stronger reactivities of the delayed type followed. This was explained on the basis of transfer of picryl chloride into a complete antigen with collagen derived from new peritoneal tubercle formation. Sensitizing injections were given to guinea pigs, using procollagen in addition to Freund's adjuvant, on days one, three, five and eight. The animals were challenged four weeks later with a single percutaneous application of 1 drop of 1.5% picryl chloride in olive oil. The reaction intensities using picryl chloride with procollagen and Freund's adjuvant were equally high; those using picryl chloride in saline and procollagen alone were low. It is concluded that haptens form cross-links with different kinds of proteins depending on the type of exposure. They cross-link with fibrous proteins when in contact with the epidermis and with globular proteins when inhaled or ingested.

Chemical Nature of the Eczematogenic Agent in Oil of Turpentine, II. Veikko Pirila and Eero Siltanen (Univ. of Helsinki) attempted to isolate the peroxide from autoxidized Δ-pinene (obtained by fractional distillation from Finnish sulfate oil of turpentine). By vacuum distillation the peroxide could be concentrated in the distillation residue, by high vacuum distillation in the last fractions and by column chromatography in the last eluates. The highest concentrations obtained were 63, 82 and 68% respectively. Skin testing of patients sensitive to oil of turpentine showed that by all these methods the eczematogen was concentrated about parallel with the peroxide.

The autoxidation and eczematogen formation could be inhibited for over seven months by adding anticatalysts (hydroquinone, pyrogallol) but, as soon as peroxide was formed despite the anticatalysts, the eczematogen also appeared. These and other similarities in the formation and decomposition of the peroxide and eczematogen suggest that the eczematogen and peroxide are identical or closely related. However differences between changes in peroxide and in eczematogen contents were found, e.g., in oxidizing samples

(4) Dermatologica 111 1-12, 1955.

perficial Skin applications of C^{14} labeled dinitrochlorobenzene (DNCB) during the interval between a sensitizing inoculation and acquisition of delayed skin sensitivity (five to six days) showed that applications one to two days old were effective elicitors of the allergic response, but that older ones were ineffective. It was inferred that only those dinitrophenyl protein conjugates in the basal viable layers are essential to development of inflammatory response Such layers are also the characteristic site of lesions evoked by patch tests with tuberculin and simple chemicals

► [Eisen's studies for the first time identify the constituents of the epidermal proteins of guinea pigs which react with specific chemically reactive allergenic groupings.

The statement that only those dinitrophenyl protein conjugates in the lower viable layers of the epidermis are essential to the development of the inflammatory response remains to be proved. After all, in the spontaneous flare-up phenomenon which occurs in sensitizations to DNCB, the allergenic material which has been applied to the skin 5-21 days previously is capable of eliciting an often very severe reaction. It still is to be ascertained whether the remnants of DNCB-conjugate are stored in the cutis or in the epidermis and, if so, where in the epidermis.—Eds.]

Significance of Cross Links in Formation of Hapten Carrier Complexes, particularly in relation to development of contact type or anaphylactic type sensitization is discussed by R. L. Mayer[3] (Summit N J) Strong sensitizers of low molecular weight combine with certain body constituents, keratin and collagen in the skin and albumins and globulins in the blood, with formation of characteristic cross links, and the transformation of a hapten into a complete antigen is identical with the tanning process Such sensitizers are formaldehyde chromate salts and compounds of quinone structure. Complete antigens leading to a contact type sensitization contain fibrous proteins keratin or collagen whereas those producing the immediate type of sensitization contain globular proteins albumin or globulin Contact antigens are viscous or insoluble since they cross link with rigid proteinic macromolecules anaphylactic or atopic antigens" are much more soluble due to cross links with nonstructural proteinic macromolecules. The concept of multiple complete antigens arising from the same hapten has many implications.

Picryl chloride regularly produced guinea pig sensitizations of the delayed type after epidermal or intradermal but

(3) Internat. Arch. Allergy 8 115-129 1956.

not intraperitoneal, application. However when intraperitoneal administration of picryl chloride was combined with Freund's adjuvant, a water-in-oil emulsion in which killed mycobacteria are suspended, many more and stronger reactions of the delayed type followed. This was explained on the basis of transfer of picryl chloride into a complete antigen with collagen derived from new peritoneal tubercle formation. Sensitizing injections were given to guinea pigs, using procollagen in addition to Freund's adjuvant, on days one, three, five and eight. The animals were challenged four weeks later with a single percutaneous application of 1 drop of 1.5% picryl chloride in olive oil. The reaction intensities using picryl chloride with procollagen and Freund's adjuvant were equally high; those using picryl chloride in saline and procollagen alone were low. It is concluded that haptens form cross-links with different kinds of proteins depending on the type of exposure. They cross-link with fibrous proteins when in contact with the epidermis and with globular proteins when inhaled or ingested.

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(4) Dermatologica 113:1-12, 1956

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eral neuroplegic compounds in the diencephalon probably is about the same. The inhibition of eczematous sensitization by serpasil[®] therefore probably is not due to its sedative and hypnotic effect on the brain stem. Rather one must consider other pharmacodynamic effects which are peculiar to serpasil (blood pressure-lowering action sympathicolytic action)

► [These results are indeed interesting and make further studies desirable regarding the mode of action by which serpasil[®] exerts this effect. To judge from our clinical experience, serpasil does not have an inhibitory action on the dermatitis in patients with allergic eczematous contact-type dermatitis. This fits in with Schnyder and Storck observation that serpasil does not depress existing allergic eczematous sensitivity.—Eds.]

Immunologic Studies in Lymphoblastomas II. Ability to Develop Eczematous Sensitization to a Simple Chemical and Ability to Accept Passive Transfer Antibody A. Rostenberg Jr H C. McCraney (Univ of Illinois) and Samuel M Bluefarb[6] (Northwestern Univ) compared patients with lymphoma leukemia diseases with a group of patients with other chronic diseases to determine their ability to develop eczematous sensitization to a simple chemical. A 10% acetone solution of 2,4-dinitrochlorobenzene (DNCB) was applied to a quarter-sized area of normal skin on the volar surface of each arm. Three weeks later 0 1 cc. 1 1000 acetone solution of DNCB was applied to another skin area and observed for 72 hours. Passive transfer studies were done, using two human serums known to contain passive transfer antibodies against guinea pig serum and against a ragweed protein extract.

Of 31 patients in the lymphoma-leukemia group in whom an attempt was made to develop eczematous sensitization, only 1 showed clear sensitization and none exhibited spontaneous flare-up. Of 14 controls, 4 showed eczematous sensitization reactions with 3 spontaneous flares. All 10 lymphoma leukemia patients on whom passive transfer was attempted accepted the antibody normally

It believed that the first step in this type sensitization is conjugation of the simple chemical with body proteins probably epidermal. Next, the conjugated protein causes an enzymatic adaptation in primitive reticulum cells and their progeny i.e the lymphoreticular cell system. When the simple chemical is re-encountered and reconjugated, the host

(6) J Invest. Dermat. 26 239-2 6, March, 1956.

at 113 F Further studies suggested that the oxidation products of Δ^3-carene, which is an important constituent of oil of turpentine and is also present as an impurity in a pinene, are responsible for the eczematogenic effect of oil of turpentine and of the terpenes distilled from it.

Experimental Studies on Effects of Neuroplegic Compounds on Eczematous Skin Reactions were made by U W Schnyder and H Storck[5] (Univ of Zurich) It was previously found that eczematous sensitization in guinea pigs to dinitrochlorobenzene (DNCB) could be prevented when the vegetative nervous system was suppressed during the sensitization period by a ganglion blocking agent The present series of experiments was carried out to determine whether neuroplegic compounds effective on the diencephalon e.g serpasil ® chlorpromazine, NP 207 influence eczematous sensitization to DNCB in guinea pigs Serpasil® is an alkaloid of Rauwolfia serpentina chlorpromazine and NP 207 are phenothiazine derivatives

In white female guinea pigs weighing about 300 Gm a 5% solution of DNCB was painted on an 8 sq cm area on the flank to produce sensitization. The animals were challenged on the 9th day after sensitization with 0.25% solution of DNCB and the reading made 24 hours later Neuroplegic compounds were instituted 1 2 days before sensitization and continued for 11 successive days with 0 05-0 1 mg serpasil® given subcutaneously every other day in 18 animals 8 mg chlorpromazine three times daily by mouth for 8 days followed by 5 mg three times daily for 3 days and 5 mg NP 207 three times daily by mouth were given in 8 animals

On the ninth day after sensitization it was found that of 15 animals still receiving serpasil ® 1 showed no reaction when challenged, 13 a very faint reaction and 1 was slightly sensitized On the 16th day (i e 6 day after serpasil® was discontinued) five of these animals were tested again and showed the same results The other 10 were retested after 30 days 1 showed a very weak reaction and 9 a reaction weaker than that of control animals

It is concluded that eczematous sensitization to DNCB in guinea pigs is inhibited by serpasil® and not influenced by chlorpromazine or NP 207 The site of action of the sev

(5) Dermatologica 112 419-425 Apr June, 1956

ternate days for 10 exposures, with a challenge application 2 weeks after the 10th test application. A chemical substance heretofore not used on the skin was capable of producing sensitization by percutaneous application. This was 2-nitro-2-bromo-1-methoxy-1-phenylpropane which was used as a 1% concentration in water-soluble ointment base. Also used, were 1% and 5% solutions in mineral oil. The reactions indicating sensitization were erythema, infiltration, papules, vesicles and, occasionally, bullae.

About equal numbers of 121 subjects were studied in each procedure. Of these 17 (14%) became sensitized. They were 19% in A, 4% in B, 32% in C, 10% in D and 4% in E. It is concluded that the effectiveness of procedure C in yielding the highest incidence of sensitization can be attributed to the prolonged (seven day) patch test and to the distribution of the patch test sites over a small area of skin four patches about 2-3 in. from each other. For more adequate evaluation, it is suggested that further studies be made with a larger number of subjects.

► [The stunning differences in the incidence of allergic sensitization resulting from the various techniques of exposure once more point out the difficulties inherent in any type of "prognostic" test procedures. Moreover it demonstrates the unbelievable variety of factors which must be determining the occurrence of allergic sensitizations, aside from the sensitizing potential of the allergen and the degree of susceptibility to sensitization of each particular patient. Within these very wide limits, studies such as this may lead to more dependable prognostic types of testing to ascertain the sensitizing index of a given substance.—Eds.]

Mortality and Skin Transplantability in X-Irradiated Mice Receiving Homologous and Heterologous Bone Marrow. J. J. Trentin[1] (Univ. of Texas) undertook to determine the relative degree and duration of protection afforded by isologous, homologous and heterologous bone marrow suspensions in x-irradiated mice and to extend the observations of Main and Prehn on skin homografting.

Results showed that the degree and duration of the protection afforded by these bone marrow suspensions administered to mice after lethal doses of x-radiation were directly proportional to the closeness of the genetic relationship of the donor to the irradiated mice. Irradiated mice protected with marrow from F_1 hybrids of the irradiated strain showed high degree and long duration of tolerance of skin homo-

1) Proc. Soc. Exper. Biol. & Med. 92:688-693, Aug.-Sept. 1956.

cells with specific enzymatic adaptations produce an eczematous response The authors previously showed that patients with lymphomatous disease have much less ability to produce delayed tuberculin type skin reactions In this study the attempt has been made to eliminate the factor of general debility associated with chronic wasting illnesses in which cases failure to develop sensitization might merely express general nonreactivity (negative anergy) Results indicated that illness per se does not prevent sensitization to a simple chemical but this conclusion is qualified by the statistically small number of patients used Previous studies with the tuberculin type reaction and the present study in which the lymphoma leukemia group showed impaired ability to develop an eczematous sensitization to a simple chemical suggested that effects could be specifically ascribed to the action of the disease process on the cells of the reticuloendothelial system It is suggested that the lymphomatous process may prevent these cells from acquiring the necessary enzymatic adaptation that it is not maintained once acquired or that the cell is unable to pass the adaptation on to its descendants There was evidently no impairment of the ability of lymphoma leukemia patients to accept passive transfer antibodies and develop a normal urticarial reaction at the site of fixation of such antibodies when exposed to the appropriate allergen

► [This study suggests strongly that in lymphoma-leukemia patients there is an inability to develop allergic eczematous sensitization and this inability is not simply based on debility or cachexia. The results with respect to acceptance of passive transfer by lymphoma leukemia patients are very difficult t interpret, since the passive transfer tests involved urticarial rather than eczematous reactions.—Eds.]

Sensitization of Human Skin Study of Location of Sites and of Exposure Time of Excitant is reported by Max Grolnick[7] (Brooklyn) Variations in technics of sensitization were (1) short and prolonged patch test exposures (2) their frequency of application (3) their total number and (4) their distribution on various areas of the body Four variations in procedure (A B C and D) were established, based on previous experiments of the author and other workers and a fifth procedure (E) was suggested by the Food and Drug Administration and these were compared with the Draize technic in which patch tests were applied for 24 hours on al

(7) J Allergy 26:542 552, November 1955

erythrocyte-epidermal cell agglutination is possible because both cell types possess a common antigen. It is postulated by R. R. A. Coombs, Donald Bedford and L. M. Rouillard[1] (Cambridge) that if skin epidermal cells of a person from blood group A possess the A antigen assuming that ordinary agglutinating antibodies are at least bivalent then such epidermal cells should be capable of being linked by anti-A to group A red cells. The general procedure used for testing epidermal cells for the A and B antigen is as follows.

METHOD.—A suspension of a group A individual epidermal cells is exposed to anti A, and the cells are subsequently washed free from uncombined antibody. Only epidermal cells with the A antigen should adsorb anti-A and consequently after being washed, possess free extending "receptors" with an affinity for the A antigen. Group A red cells added at this stage should combine with the extending anti-A receptors on the treated epidermal cells. On the other hand, group B and group O red cells should not adhere to the treated epidermal cells. The skin used consisted of small fragments of stored split-thickness skin procured for plastic surgery. The epidermal cells were prepared by the tryptic digestion process of Medawar.

The results offer conclusive evidence for the existence of the A and B antigens on epidermal cells of group A and group B persons, respectively. Anti-A is adsorbed on epidermal cells of group A persons only and similarly anti-B is adsorbed on epidermal cells of group B persons only. Nine group A, five group O and three group B subjects were examined. The tube containing group O cells is a good control for any nonspecific agglutination which occurred in one instance in which the epidermal cells were contaminated with bacteria.

These findings are of significance in the problem of skin homografts. Skin cells should be examined with specific serums for other blood group systems and an attempt made to establish their full antigenic structure and to determine which of the intra-species antigens are concerned in the homograft reaction. These observations also may be important in forensic medicine, because it may be possible to identify the A-B-O group of an isolated piece of skin completely devoid of blood. The method has also been applied to confirm the presence of A and B antigens on platelets and probably could be used with most tissue cells, affording a useful tool in studies of the antigenic architecture of tissue cells in general.

(1) Lancet 1:461-463, Apr. 21, 1956.

grafts from F_1 hybrids or from the other parent strain. Irradiated mice protected with foreign strain mouse marrow showed a high degree and long duration of tolerance to skin homografts from the same foreign strain. However irradiated mice protected with marrow from the same strain did not tolerate skin homografts from a foreign strain or from an F_1 hybrid

Demonstration of Tissue Autoantibodies in Blood Serum of Patients with Certain Skin Diseases. The main pathologic change in lupus erythematosus lies in fibrinoid degeneration of connective tissue, and the literature reveals some evidence that allergic reaction and autoimmunization may be a starting mechanism for the disease Vladimír Wagner and George Seba[9] (Univ of Pilsen) studied three patients with lupus erythematosus two with pemphigus vulgaris one with acrodermatitis chronica atrophicans and one with impetigo herpetiformis of Hebra The serum was tested using collodion agglutination Tissue antigens were from persons who had recently died of noninfectious diseases Controls were (1) collodion particles alone (2) collodion particles coated by antigen (3) collodion particles coated with antigen and negative serum and (4) collodion particles without antigen, but with tested serum diluted as in the main experiment i e. geometrically the end point being the dilution in which visible agglutination still appeared.

The relation of serologic and clinical findings was almost quantitative, i e the higher the titer of autoantibodies the more the respective tissue was affected With this technic serums of clinically healthy persons gave no reaction Thus the autoantibodies reflect a real pathologic process and serve as an indicator of its activity This change may be of prognostic value also since the autoantibodies can be demonstrated before the appearance of organic symptoms These findings support Klemperer's theory of collagen diseases and the hypothesis of an immunotoxic mechanism of pathogenesis.

► [It appears likely that autoantibodies will attract increasing attention in dermatology as well as in other categories of medicine in the years to come. Their presence may help explain certain hitherto poorly understood clinical events and dermatologic syndromes.—Eds.]

A and B Blood Group Antigens on Human Epidermal Cells Demonstrated by Mixed Agglutination. Mixed

(9) Dermatologica 112:25-36, January 1956.

erythrocyte-epidermal cell agglutination is possible because both cell types possess a common antigen. It is postulated by R. R. A. Coombs, Donald Bedford and L. M. Rouillard[1] (Cambridge) that if skin epidermal cells of a person from blood group A possess the A antigen assuming that ordinary agglutinating antibodies are at least bivalent then such epidermal cells should be capable of being linked by anti-A to group A red cells. The general procedure used for testing epidermal cells for the A and B antigen is as follows.

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(1) Lancet 1:461-463, Apr. 21, 1956.

► [An excellent contribution from the immunologic and technical viewpoints, identifying one of the factors which lends the skin its specific immunologic "tag." Among the many important questions arising from these findings is: Do the cells of hair and nail also possess specific blood group antigens or have they lost this part of the antigenicity of skin cells?—Eds.]

Local Anaphylactic Changes in Rabbit Ears With Special *Reference to Anaphylactic Hyperkeratosis and Papillomatosis* and Survey of Mechanism. O. Reuterwall[2] (Kadrumhemmet, Stockholm) observed that when the same anaphylactogen was repeatedly given for long period, anaphylaxis could follow three different courses. If dosage was too high the general condition of the rabbits was affected and cachexia of Arthus appeared. With lower dosage the anaphylaxis followed a law bound course with certain well defined stages. Still lower dosage was associated with irregular fluctuations of anaphylaxis which even long after could reach considerable intensity. This did not agree with the old experience of *recession of anaphylaxis after protracted repeated* anaphylactogen administration. The toleration limit varied in different rabbits.

In rabbits given injections twice weekly of 1 cc of 2 10% serum or egg white, the following stages of anaphylaxis could be distinguished: incubation period, increasing anaphylaxis, highly anaphylactic stage, declining anaphylaxis, residual anaphylaxis, and precipitin free final stage. Anaphylaxis followed these stages in rabbits that were good precipitin producers and in those that were less good in this respect. Only exceptionally did the precipitin titer rise briefly when anaphylaxis had come far down the scale. The precipitin free stage was not reached for a long time. When smaller anaphylactogen doses (1 cc of 1%) were injected semiweekly, anaphylaxis did not follow the regular course and division into stages could not be made.

Research earlier concentrated on the classic Arthus phenomenon with necrosis. However, local anaphylactic reaction includes not only hyperemia, edema and necrosis, but loss of hair, hyperkeratosis, papillomatosis, gloss, skin crusts and pigment change. In the rabbit skin of different regions reacts in considerably dissimilar fashion.

To maintain a local anaphylaxis at optimal proliferation

(2) Acta dermat.-venereol. vol. 36, supp. 36, 1956.

promoting intensity for a long time the anaphylactogen dosage which will exert suitably strong local action should be decided on and antibody production kept on a sufficiently high level.

As far as could be judged from the histologic picture a considerable antibody production gradually takes place in a tissue area into which anaphylactogen is repeatedly injected. The antibody-forming cells were apparently derived mainly from perivascular and similar perifollicular cells. Connective tissue cells in general however seemed also to join in this process. Many plasma cells and their precursors appeared. When antibody production, as judged from determination of blood serum precipitin approached or reached its end, plasma cells disappeared more or less completely.

Theoretically in local anaphylactic experiments stimulation traceable to anaphylactogen-antibody union and to products of that union may be presumed to be due to physical condition changes of which precipitation is an expression and also derives from disintegration products of parenteral digestion. How this stimulation to reaction takes place is still uncertain.

Comparative experiments with the carcinogens, tar and dibenzanthracene were carried out. Solutions of these substances in olive oil were injected into the rabbit ear similarly to native anaphylactogens. One injection of 0.5 cc. of 1% tar in olive oil evoked protracted proliferation of epidermal cells. In the day immediately after injection, this was severe and the boundary between epithelium and connective tissue confused. Rate of proliferation then moderated and gradually papillomatosis developed which closely resembled that in the anaphylaxis experiments. Skin tests showed that reactivity to tar and dibenzanthracene was unchanged, even after these had been injected many times. Tar and dibenzanthracene clearly acted directly without antibody intermediation.

Cutaneous Allergies and Histamine. Allergic phenomena can be divided into immediate and delayed reactions. In the former group (asthma urticaria-anaphylaxis type) clinical symptoms appear immediately after antigen is administered and cutaneous wheal with or without inflammatory changes are seen. Hypersensitivity can be transferred with serum. In the latter group (experimental contact dermatitis-tuberculin

reaction type) clinical symptoms appear after an interval of several hours and humoral antibodies do not exist i.e., hypersensitivity can be transferred only with white blood cells, not with serum Histamine set free in the tissue was assumed to be the cause of immediate, but not of delayed reactions since the latter could neither be produced by injection of histamine nor influenced by antihistamines.

Experiments carried out by Theodor Inderbitzin[3] (Univ of Zurich) revealed the following facts (1) Both immediate and delayed reactions change the histamine contents of the skin of guinea pigs (2) Immediate reactions induce an immediate rapid fall of skin histamine about 50% of normal values in cutaneous anaphylaxis 30% in the Arthus phenomenon In the latter this initial phase is followed after about six hours (i.e. with onset of inflammatory changes) by a local histamine increase of about 200% (from 3 to 9 μg histamine/Gm tissue) The initial decrease in tissue histamine cannot be explained Histamine liberated from the skin most likely originates from mast cells (3) Delayed reactions produce no immediate change in skin histamine values during the free interval but these values begin to rise slowly after 3-6 hours show a markedly accelerated increase after 12 hours with a peak after 48-72 hours and return to normal in 96-120 hours (4) The increase in tissue histamine contents *in eczematous or tuberculin allergic reactions* coincides with the local inflammatory reaction which consists mostly of a mononuclear cell infiltration (5) Polymorphonuclear neutropenia neither alters the clinical response nor the local histamine increase whereas lymphopenia suppresses both. Nothing certain is known about the function of the increased histamine in the sites of reaction.

Effect of Sarcoidosis Serums on Tuberculin Response was investigated by Bertil Magnusson[4] (Karolinska Hosp Stockholm) By applying a mixture of tuberculin and sarcoidosis serum to a tuberculin sensitive recipient according to the methods of Pirquet or Mantoux and comparing the result of this test with a tuberculin control of similar strength applied at the same time, other workers have studied the effect of sarcoidosis serum on the tuberculin reaction. Though the findings have often been conflicting most writers have

(3) Dermatologica 112 435-443 Apr June 1956.
(4) Acta dermat.-venereol. vol 36, supp 35 1956.

claimed to have demonstrated an inhibitory effect. This "tuberculin-neutralizing" effect has been ascribed to substances of antibody nature present in sarcoidosis serum. Magnusson performed the Mantoux test using a mixture of tuberculin and sarcoidosis serum, on 210 tuberculin-sensitive patients.

Among all experiments performed with sarcoidosis sera, a depressed reaction was obtained in 11.7% compared with 14.1% among controls. No significant difference could be demonstrated in incidences of enhanced, unchanged and depressed reactions between the sarcoidosis series and the control or between all Mantoux negative and all Mantoux positive test serum donors.

No factors (anticutins) could be demonstrated in the serum of patients with sarcoidosis which influence the tuberculin reaction. However it was shown that the extent of the reaction to the tuberculin-serum mixture at 48 hours could be correlated with the response to the mixture at 15 minutes and with the tuberculin control at 48 hours. The gist of the problem of procutins and anticutins, which in earlier investigations entirely centered on the serum donors, is therefore now transferred to the recipients. This new interpretation of the anticutin problem is compatible with other experimental work on allergy.

[These studies recall those of Cole and Favour (J. Exper. Med. 101 391 1955) and Wells and Wylie (Lancet 256 439 1949). In passive transfer experiments of tuberculin sensitivity Cole and Favour reported that the antibody which produces the delayed 48 hour type reaction was inhibited when the antibody mediating the immediate urticarial type reaction was also present in the transferred serum. Wells and Wylie described tuberculin-neutralizing factor.—Eds.]

Intradermal Test in American Leishmaniasis with a Polysaccharide Fraction Isolated from Leishmania Braziliensis. Tancredo A. Furtado and J. Pellegrino[1] (Belo Horizonte Brazil) compared two types of antigens for intradermal test in leishmaniasis (1) polysaccharide fraction isolated from culture forms of Leishmania braziliensis (2) suspension of leptomonas containing 10,000,000 flagellates/ml. Tested were 21 patients with American leishmaniasis and 45 controls, including 10 normal persons and 35 with miscellaneous dermatologic conditions.

In the leishmaniasis group reactions with the polysaccha

(1) J. Invest. Dermat. 27:53 59 August, 1956.

ride fraction were positive in 17 patients and with the suspension of leptomonas in 18. In the control group the suspension caused false positive reactions in five patients two with lepromatous leprosy one with scrofuloderma, one with pemphigus foliaceus and one with South American blastomycosis Results with polysaccharide fraction were always negative.

The study showed that the intradermal test with polysaccharide fraction is comparable in sensitivity to the reaction obtained with suspension of leptomonas in patients with American leishmaniasis but is more specific The polysaccharide antigen is preferable particularly in regions where leishmaniasis is endemic and differential diagnosis with various tropical dermatoses is of great importance.

Studies on Dissemination of Fungi from Feet of Subjects with and without Fungous Disease of Feet were made by Stanley A. Rosenthal Rudolf L. Baer Jerome Z Litt, Hymen Rogachefsky and Domenica Furnari[6] (New York Univ Post-Grad Med School and Skin and Cancer Unit) The study included 91 subjects with clinical evidence of fungous disease of the feet and 40 without such evidence The feet were entirely bathed with 70% alcohol and then immersed in 200 ml sterile water for 15 minutes The sediment was centrifuged examined microscopically and cultured on Sabouraud s dextrose agar

Fungi were readily shed into foot baths from the feet of 73.6% of subjects with clinical signs of fungous disease and from 12.5% of those without Routine mycologic scrapings yielded a slightly higher number of positive microscopic results and a markedly greater number of isolations in culture than foot soakings Hotchkiss McManus stains were slightly superior to KOH mounts in detecting fungous filaments in foot bath sediments Mediums containing cycloheximide penicillin and streptomycin were superior to all other in isolating dermatophytes from foot bath sediments. Extensive attempts to isolate pathogenic fungi from public shower stalls, locker room floors and area around swimming pools have been entirely unsuccessful The results indicate that viable fungi must be readily shed from clinically or subclinically infected feet and that frequent exposures and re-

(6) J Invest. Dermat. 26 41 51 January 1956.

exposure to these fungi is practically inescapable and unpreventable.

Experimental Investigations on Mechanism Producing Acute Dermatophytosis of Feet were carried out by Rudolf L. Baer, Stanley A. Rosenthal, Jerome Z. Litt and Hymen Rogachefsky (New York Univ. Post-Grad. Med. School and Skin and Cancer Unit) to determine the role of exogenous exposure in the causation of acute attacks of fungous disease of the feet. Two approaches to the problem were made.

The first experiments attempted to determine whether foot bath water contaminated with pathogenic fungi can produce acute attacks of dermatophytosis in subjects clinically and mycologically free from the disease. A group of 68 uninfected volunteers was studied. Of these 14 immersed the right foot, for 30 minutes, in 200 ml. water infected by previous soaking of both feet of a subject with fungous disease for 15 minutes. The left foot of the volunteer was a control, immersed in 200 ml. sterile water also for 30 minutes.

Fungi were proved to be in the right foot basin by direct examination and smear and stains. The other 54 uninfected volunteers carried out the same procedure but contamination was by direct addition of fungous culture material. Weekly follow-up examinations were done six times. Not a single instance of clinical fungous disease was produced although fungous mycelia were found in one or both feet of 37 (54%) during the six weeks after exposure (in 19 on the exposed feet, in 5 on the control foot and in 13 on both feet). The common dermatophytes are considered to be facultative pathogens or opportunists that may be on healthy skin for a time. Only when conditions for growth become favorable may clinical disease result.

The second group of experiments was conducted to determine if the feet of subjects with a primary fungous infection due to one species of dermatophyte could be deliberately superinfected with another species of dermatophyte. The feet of 20 infected volunteers were immersed for 30 minutes in a foot bath heavily contaminated with fungi. In 4 of the 20 a culturally proved fungous superinfection was produced. Results suggest that feet with fungous disease are inherently more susceptible than those free from clinical fungous disease.

J. A. M. A. 160:[illegible], Jan. 21, 1956.

It is desirable to differentiate between "asymptomatic fungous infection" and "fungous disease" of the feet. Public health and individual measures for prevention of attacks of fungous diseases must be based on the maintenance and increase of local resistance to infection of the feet rather than on largely useless measures to prevent infection.

► [These findings point out, once again, the false security and lack of protection against fungous disease likely to be derived from the medicated foot baths found in shower and locker rooms. Likewise they stress the importance and the benefits to be gained from proper care of the feet in the attempt to lessen the tendency toward active fungous disease.—Ed.]

Influence of Adrenocortical Hormones on Dermatomycoses, Especially in Cushing's Syndrome was studied by G. Cremer[8] (Univ. of Amsterdam). Earlier animal experiments showed no conclusive effect but pointed to some decrease of resistance. Two patients with dermatomycoses were treated for purpura with adrenocortical hormones and subsequently showed Cushing's syndrome.

Case 1.—Man, 27, had a fungous infection of the feet for four years and similar less severe affection of the hands for one year. While treatment was most intense a typical Cushing syndrome developed, and the mycosis spread to the hairs of the pubis and the scalp until the latter was almost entirely involved. There was little inflammatory reaction on the skin itself, whereas in four nurses who were infected by the patient the skin reaction was much greater. Trichophytin reaction was absent in the patient and present in the four contact patients.

Case 2.—Woman, 65, had had tinea capitis as a girl. At the height of adrenocortical steroid treatment, she had considerable extension on the hairy scalp and skin of the face, trunk and limbs, but the skin reaction itself was minimal.

Two patients who had extensive dermatomycoses also had Cushing's syndrome as a result of adrenal tumors. Both were relieved of the dermatomycoses after surgical excision of the tumors. The connection between the extensiveness of the mycoses and Cushing's syndrome appeared clear in these four patients. Decreased resistance existed to the fungi cultured, Trichophyton tonsurans, T. rubrum, T. mentagrophytes, T. interdigitale and Candida albicans.

In Cushing's syndrome, adrenocortical hormones cause a much decreased resistance to fungi, which is shown by the following findings: (1) wide scalp extension of the mycoses in adults, (2) the slight inflammatory reaction of the patches

(8) Dermatologica 111:285-293, November, 1955.

compared with the infection in contact persons, (3) resistance to antimycotic therapy unless steroid therapy was reduced or adrenal tumors removed, and (4) repeatedly absent trichophytin reaction in contrast to the reactions present in the restricted contact infections.

Prolonged treatment with ACTH or cortisone should be limited to patients in whom it is essential. It is desirable when beginning treatment to find out if the patient has a dermatomycosis and to treat it at once.

► [An interesting finding but a circumstance which must be quite rare. We have treated many hundreds of patients with systemic corticosteroids without evidence of spread of an existing dermatomycosis. Certainly some *of these patients must have had an active mycotic infection* of the feet or groin (see this YEAR BOOK, pp. 362 and 363). Neither have we been told by any of our colleagues of any cases of remarkable extension of superficial fungous infections, even in patients on large and prolonged doses of corticosteroids.

Infection of four nurses by the one patient with T. mentagrophytes infection is also unusual. More details about the clinical features of this epidemic would have been desirable.—Eds.]

Comparison of Littman and Cycloheximide Mediums for Primary Isolation of Dermatophytes is presented by Edward M. Shapiro, J. Fred Mullins and Mary E. Pinkerton[9] (Univ. of Texas).

METHOD.—Two sets of Petri plates were used, one set containing Littman oxgall agar to which had been added 30 units/ml. streptomycin and 0.001% crystal violet to inhibit bacterial contamination, and the other set containing cycloheximide medium, prepared from Sabouraud's dextrose agar to which 20 units/ml. penicillin, 40 units/ml. streptomycin and 0.5 mg./ml. cycloheximide were added after the agar was autoclaved. Duplicate cultures were taken from patients with suspected superficial fungous infections and all duplicate plates were incubated at room temperature.

From 53 duplicate cultures 30 pathogenic fungi were isolated on one or both mediums. Three organisms were found only on Littman's: Trichophyton rubrum, T. tonsurans and species of trichophyton. Three were isolated only on cycloheximide: T. mentagrophytes, Candida albicans and a species of trichophyton. In all, 28 cultures failed to grow pathogenic fungi on Littman's and 27 on cycloheximide agar. Cycloheximide yielded fewer saprophytes, and the morphology of the fungi was the same as on Sabouraud's agar. The dermatophytes were identified more rapidly on Littman's agar and growth was initiated earlier. On Littman's, saprophytes were a problem only in grossly contaminated specimens

(9) Am. J. Clin. Path. 24:124, February 1954.

mens Petri plates should be used instead of test tubes with Littman's medium Littman's agar is preferable for routine use in the isolation of dermatophytes although cyclohexi-mide agar is of supplementary value especially when sapro-phytic contamination is suspected

► [Studies at the New York Skin and Cancer Unit by S. Rosenthal *et al* (J Invest. Dermat. 26 41 1956) showed cycloheximide containing cultures much superior to Littman's agar in the isolation of dermato-phytes.—Eds.]

Study of pH Changes by Molds in Culture Mediums : pre-sented by Norman J Goldfarb and Franz Herrmann[1] (New York Univ Post Grad. Med School and Skin and Cancer Unit) A universal pH indicator was added to culture me-diums of various molds including several species of derma tophytes and several saprophytic species In mediums of cul-tures obtained from different strains of 11 species of dermato-phytes a distinct shift in pH toward alkalinity was observed at and around the site of growth In mediums of different "common laboratory contaminants " a distinct acid shift was observed in nearly all in the same area only occasionally was no change in pH discernible in a priori acid medium Characteristic degrees of the shifts in pH were obtained with different species in both groups

The pH changes in the medium were apparent shortly after start of visible growth of dermatophytes and sometimes preceded visible growth of saprophytes These changes per mitted early differentiation between pathogenic and non pathogenic mold and facilitated selection transplantation and isolation of pathogens from contaminated cultures

Zones of alkalinization or acidification were sharply de-lineated In mixed culture of dermatophytes and sapro-phytes areas of opposite ranges in pH remained clearly sep-arated At the junction of the two areas a borderline formed, on one side of which the medium was alkaline and on the other acid subsequently a sharp band of near neutral pH developed—and for some time widened—between the two zones These areas and delineations are due to formation of electric border equilibriums known to result from dif fusion of alkaline and acid electrolytes through gelatinous substances

► [Any procedure which would permit the early selection, transplantation and isolation of pathogens from contaminated cultures would be a worth while addition to mycologic laboratory routine —Eds]

(1) J Invest. Dermat. 27 193-201 September 1956.

Mycologic Study on Interdigital Mycoses Animal Experiments and Analysis of Antigens. Epidermophyton kaufmann Wolf and E. rubrum Castellani, the principal micro-organisms causing interdigital mycoses have recently been included into th trichophyton group because of clinical analogies (both epidermophytons were reported to invol e hair in rare instances) and morphologic-cultural similarities. Whether any biologic conformities also exist between these epidermophytons and the trichophyton species was in estigated by Emil Fischer[2] (Univ of Zurich)

1 Guinea pigs were inoculated with various cultures of E. kaufmann-Wolf and E. Castellani It was seen that these fungi hitherto often called epidermophytes in olve ha r just as f ngi of the trichophyton group The only true epider mophyton, therefore is E. inguinale (or floccosum)

2 Intracutaneous tests with trichophytin and epidermophytin in epidermophyton and trichophyton nfected guinea pigs were positive n all nimals. Independently of whether epidermophyt n or trichophyton fungi were used for noculation, the ntracutaneous epidermophytin reaction was generally stronger than the trichophytin reaction. Since trichophytin and epidermophytin reactions a e group-specific, no diagnostic con lusions can be drawn as to the nature of the fungus used for animal inoculation.

3 For analysis of antigens, i.e whetl er dry trichophytin of E. kaufmann-Wolf nd E. Castellani can be differentiated from dry trichophytin f Trichophyton gypseum the Schultz Dale experiment with uterus horns of guinea pigs sensitized with dry trichophytin of epidermophyton and tribophyton fungi was used. Dry trichophytin contain not only partial antigens common to many fungi but also specific pecies ant gens. The latter are different in epidermophyton and trichophyton fungi the antigen structure of dry tri hophytin is different, not only between various epidermoph ton fungi but also particularly between epidermophyton and trichophyton fungi. Antigen analysis therefore showed that epidermophyton and trichophyton fungi are not identical.

It was observed long ago that mycelia of fungi of the same pecies may on contact in the culture form anastomoses (fu

(2) Arch f. klin. [illegible] Dermat 303 278-318, 1934.

mens Petri plates should be used instead of test tubes with Littman's medium Littman's agar is preferable for routine use in the isolation of dermatophytes although cycloheximide agar is of supplementary value, especially when saprophytic contamination is suspected.

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Zones of alkalinization or acidification were sharply delineated In mixed cultures of dermatophyte and saprophytes areas of opposite ranges in pH remained clearly separated. At the junction of the two areas a borderline formed. on one side of which the medium was alkaline and on the other acid subsequently a sharp band of near neutral pH developed—and for some time widened—between the two zones. These areas and delineation are due to formation of electric border equilibrium known to result from diffusion of alkaline and acid electrolytes through gelatinous substances

► [Any procedure which would permit the early selection, transplantation and isolation of pathogens from contaminated cultures would be a worthwhile addition to mycologic laboratory routine.—Eds.]

(1) J Invest Dermat. 27 193 201 September 1956.

able to porphobilinogen. Should these permeability differences extend to other cells, the rapid entry of δ-aminolevulic acid into cells and its transformation, enhanced by light, to uroporphyrin could explain the brilliant fluorescence of the epidermis and its injury under irradiation. Assays of δ-aminolevulic acid and porphobilinogen excreted by patients with porphyria having cutaneous and abdominal symptoms are proposed to clarify the chemicopathologic differences between these types.

Cutaneous Changes during Menstrual Cycle. Clinical and Experimental Study under Physiologic Condition and after Therapy. Frederick Kalz and Allene Scott (Montreal) conducted a clinical and experimental study of 60 patients. 50 were premenopausal women with premenstrual tension and exacerbations of the dermatosis which was generally acne vulgaris. Control consisted of five postmenopausal women and five men; two of the men also had acne vulgaris.

METHOD.—The ovulatory cycle was identified by weight and temperature records and observations made of alterations in existing dermatoses and emotional states. The following experimental methods were used: (1) hyaluronidase and histamine wheal resorption, for measuring fluid retention; (2) measurement of size and duration of the flare surrounding the histamine wheal, for measuring vascular reactivity, and (3) osmic acid filter paper prints, to estimate activity of sebaceous glands.

In the premenopausal women, a regularly recurring pattern was observed parallel to phases of the ovulatory cycle. Exacerbation of dermatoses and increase in emotional tension occurred premenstrually. These changes were correlated with faster wheal resorption time for hyaluronidase and histamine and shorter duration of the histamine flare. Increased sebaceous gland activity was demonstrated in only about 50% of patients. Hence the skin tests, except the osmic acid test, could be used for objective observation through the phases of the menstrual cycle.

Ammonium chloride and pre-mens (containing ammonium chloride, homatropine, caffeine, vitamins B, B_2, B_6, calcium pantothenate and nicotinamide) prevented the flare of acne vulgaris and other dermatoses and controlled premenstrual tension in most patients. Pre-mens appeared to be somewhat more effective. In the controls, none of whom exhibited any cyclicity in clinical symptoms or test re-

(4) A.M.A. Arch. Dermat. 74:493-503, November 1956.

sion of hyphae ") but that this phenomenon does not occur on contact of mycelia of different fungi. Corresponding examinations did not permit any conclusions regarding the relations between epidermophyton fungi and the trichophyton group

It is believed that E. Kaufmann Wolf and E. rubrum Castellani can be included into the trichophyton group because of morphologic-cultural as well as biologic reason despite different antigen structure

► [There can no longer be any doubt about the capacity of T rubrum to produce small granulomatous as well as kerion-type lesions.

Taschdjian and Muskatblit (Mycologia 47:339 1955) used hyphal fusion as a method of demonstrating species relationship between variants of T tonsurans (T epilans or cerebriforme, T sabouraudii or acuminatum, T sulfureum) —Eds.]

δ-Aminolevulic Acid and Porphyria. The evidence of A. Jarrett C Rimington and D A Willoughby[3] (Univ College Hosp Med. School London) indicates that δ-aminolevulic acid alone is not responsible for the abdominal or cardiovascular attacks in acute porphyria. δ-aminolevulic acid is the immediate precursor of porphobilinogen. However in the cat δ aminolevulic acid in doses of 100 μg /kg did not alter heart rate or blood pressure nor did 100 μg acid in a 20 ml bath affect isolated guinea pig ileum.

Effects of δ-aminolevulic acid and porphobilinogen were compared in albino rats with and without ultraviolet irradiation The backs and sides were shaved and 10 minutes after injection of 30 mg /kg body weight these rats and uninjected controls were exposed to the carbon arc for 15 minutes at 12 in. The control and the rat injected with porphobilinogen showed no irritability or hyperemia that injected with δ-aminolevulic acid scratched, bit, shook itself and had hyperemic skin

Only combined δ-aminolevulic acid and irradiation caused photosensitivity and fluorescence in the rat so treated [illegible] the arc light [illegible] he epidermis [illegible] the transformation into porphyrin. The ease with which these substances enter the cells is dominant in determining the distribution of porphyrin after their injection Fowl erythrocytes permit ready entry of δ-aminolevulic acid but are much less perme

(3) Lancet 1 125-127 Jan. 21 1956.

(Creighton Uni) It was found in previous stu lies that stress elicits remarkable changes in capillary resistance These changes, termed capillary stress response may vary with intensity of stress diet, species and innate individual characteristics of the human being and the experimental animal under standard conditions and in most indi iduals of the same species they are rather uniform.

The authors produ ed typical skin lesions reminiscent of eczematous plaques or seborrheic dermatitis by means of various forms of stress in albino rats and guinea pigs fed normal diets. The animals simultaneously showed changes in the capillary resistance (capillary stress response) the skin lesions appearing always when capillary resistance was t low levels Whereas extrinsic factors (exposure of the skin to local rritation by removal of the hairs) were considered to play an undoubted role n exciting these lesions the presence of an ntrinsic facto produced by the stress and render ing the external factors effective must be assumed. This i postulated by virtue of the finding that in nonstressed ani mal (with normal capillary resistanc) the lesions failed to develop despite presence of the same external factors.

Two possibilities a suggested to explain the nature of the ntrinsic factor Previous studies ndicated that capil lary resi tance chi fly influenced by two hormones corti costeroids and the somatotropic hormone of the anterio pituitary the former increases and the latter dec eases it Thus the actual lev l of capillary resistance seems to be th result of a balance between these two hormones The authors suggest that the capillary stress response eflects the profound functional change n the endocrines which was eli ted by t ess. Another poss bility may be that th decreased capillary esistance tself i cited by the forementioned en docrine changes, play some rol in this skin process.

► [These investigator subjected the animals to various forms of stress, consisting of cold, heat, prolonged swimming, surgical operation, crushing one leg, fasting or ether anesthesia Each of these is indeed stressful situation, and it is not surprising that systemic reactions followed that might be effected in the skin —Eds]

Testing of Industrial Pr tective Ointments. It had been observed that repeated pplications—e.g rubbing n (as in M test) of skin-protecti e ointments—were not followed by rritation wherea patch tests with the same material re-

sponses these drugs affected neither of the manifestations.

It is thought that fluid retention is significant in premenstrual exacerbations of acne vulgaris and other dermatoses and in premenstrual tension. However other factors, perhaps emotional also appear concerned.

► [Among the other factors which are believed to play a role in the premenstrual flare-ups of acne is the upset in the balance between circulating estrogen on one hand and progesterone and/or androgen on the other about which much has been written. In our own experience as that of others, the premenstrual administration of estrogens, e g premarin, in some cases has proved beneficial in reducing premenstrual acne exacerbations. We have not been impressed with the beneficial effects obtained with ammonium chloride in premenstrual exacerbations of acne—Ed.]

In Vitro Metabolism of Testosterone by Human Skin is exceptionally high according to Herbert H Wotiz Herbert Mescon Harold Doppel and Henry M Lemon[5] (Boston) Testosterone metabolism was calculated on a cellular basis by desoxypentose nucleic acid determinations The effects of quick freezing on steroid metabolism were determined. Comparisons were made of skin from different body areas and of normal and diseased skin Biopsy tissues were obtained with a sterile 5 or 7 mm motor-driven punch without anesthesia and were incubated in a solution containing 1 mg 4-C^{14} testosterone the contents were extracted with methanol. Paper chromatography was performed and quantitative determinations were made with the Beckmann DU spectrophotometer Radioautography was performed and results were read after four weeks Total amounts of desoxypentose nucleic acid were also determined for each tissue examined.

Results of incubation of biopsy specimens from normal back sites varied only slightly Results between fresh and frozen samples differed little and freezing to permit histochemical studies seems to be a safe procedure Comparison of back axilla and scalp tissue showed only moderate personal variation but considerable differences between persons. No conclusions could be drawn from the pathologic specimens except that three patients with verruca vulgaris showed comparable metabolic rates By means of radioautography seven new radioactive- and Zimmerman positive substances were noted.

Experimental Stress Dermatitis was studied by Jeno Kramár V William Meyers and Charle M Wilhelmj Jr[6]

(5) J. Invest. Dermat. 26 113 120 February 1956.
(6) Ibid 25 275-280, October 1956

paired. There may be extensive involvement of the tonsils and pharyngeal area.

An eruption of discrete or confluent round yellowish white papules is found on the skin, most commonly on the margins of the eyelids, face, nape of neck and dorsa of hands and fingers. Bullous, pustular and crusting lesions occur. Depending on the extent and severity of involvement scarring may develop. The scars may be of the small pitted varioliform variety or appear as large, smooth, depressed and atrophic areas. Older lesions, particularly on the hands, elbows and knees, may have a distinctly verrucoid appearance.

Margaret Gray Wood, Frederick Urbach and Herman Beerman[8] (Univ. of Pennsylvania) studied histochemically the deposit in the dermal tissue of a man aged 26, with lipoid proteinosis. The performic acid Schiff reaction and application of sudan black B to the deposit indicated the presence of phospholipids or galactolipids. Results of the baker extraction test combined with the baker acid hematein method and of the Keilig extraction test suggested that the deposit in this patient may be a glycolipoprotein, possibly kerasin.

Cholinergic Innervation of Digital Arteriovenous Anastomoses of Human Skin: Histochemical Localization of Cholinesterase. Harry J. Hurley Jr. and Herbert Mescon attempted to obtain histochemical proof of cholinesterase in the nerve fibers supplying the digital arteriovenous anastomoses in five human volunteers. These anastomoses shunt blood directly from arteriole to venule parallel to the capillary bed and thus form some protective device in the heat regulation of the skin. Together with other associated blood vessels and their nerve supply they are histologically specialized structures, called glomi.

Available evidence (response to epinephrine and sympathetic stimulation) indicates that the arteriovenous anastomoses probably have an adrenergic innervation controlling their active constriction. Using punch biopsy specimens from the skin of the volar pads of the great toes of the volunteers and Koelle method, the authors found specific cholinesterase in many nerve fibers around the arteriovenous anastomoses and around the secretory tubules of eccrine sweat glands. The enzyme was absent around other cutaneous ves-

(8) J. Invest. Dermat. 26: 263-274, April, 1956.
( ) J. Appl. Physiol. 9: 82-84, July, 1956.

vealed a high percentage of positive reactions H Kuske, M Klayman and K. Schwarz[7] (Univ of Bern) therefore carried out comparative investigations with some industrial protective ointments with regard to primary irritant properties and prophylactic effectiveness In 30 persons, protective effects against primary irritant effects of alkalis (water soluble noxae) were determined by the alkali resistance test (Burckhardt) in areas treated with protective creams and in untreated control areas In another 30 persons protective effectiveness against primary irritant effects of gasoline (fat soluble noxae) was determined by patch tests with various concentrations of gasoline in areas treated with protective ointment and in untreated skin areas Protective effects against specific allergens were tested in another 30 persons.

Difference in primary irritancy were found which probably were due to the saponifying effect of individual protective ointments i e sweat and/or sebum combine with the ointment thus forming a product that causes epithelial damage The more indifferent protective ointments were also less effective. On previously diseased skin or on skin already showing the first signs of recurrent disease, protective ointments had hardly any protective, but rather exacerbating effects here the indifferent ointment bases are preferable.

Histochemical Study of Case of Lipoid Proteinosis. Lipoid proteinosis is a rare disturbance of the local lipid metabolism of the skin and mucous membranes It is characterized by early involvement of the mucous membranes and by later appearance of infiltrative plaques and nodular and hyperkeratotic masses in the skin Hoarseness develops in infancy due to involvement of the vocal cords There may be concurrent anomalies of the hair (alopecia and poliosis) and dentition (hypoplasia or aplasia of the lateral superior incisors) The course is benign unless extensive involvement results in respiratory difficulty Association with diabetes mellitus consanguinity of parents and a familial tendency have been reported.

The mucosal lesions consist of raised yellowish white diffuse or nodular infiltrations on the gums floor of the mouth, uvula soft palate, epiglottis and vocal cords. The tongue acquires a woodlike firmness and its motility is im-

(7) Dermatologica 112:316-322, Apr June 1956.

Synthetic Detergent as Provocative Agent in Patch Tests. Synthetic detergents are characterized by marked wetting effect and capacity for fat emulsification. At neutral reaction they can rapidly remove particles of dirt, and by reducing the surface tension of water they aid *rinsing and drying* of crockery. The high cleaning efficacy of these agents has abetted the impression that they might be more deleterious to the skin than soaps. To assess the role of these surface active agents in inducing eczema, S. A. Kvorning and Inge Borup Svendsen (Rigshosp., Copenhagen) performed patch tests with the synthetic detergent, teepol.

Patch tests using the commercial product only exceptionally gave rise to irritation in the form of reddening and infiltration and only at concentrations considerably higher than generally used. With soap in the same concentrations, irritation was more common.

To find whether the allergic action of water-soluble antigens is promoted by addition of a surface-active agent which brings the solute in closer contact with the skin, a series of patch tests with nickel chloride and potassium bichromate was made on patients known to be allergic to these substances. On the right side of the back, a series of tests was applied with the allergen dissolved and diluted to various concentrations in distilled water. On symmetrical sites on the left side of the back, a corresponding series was applied in which the salt was dissolved in and diluted with a 1% teepol® solution. These patch tests were removed after 24 hours. The results were read at once and again after at least a half-hour.

High concentrations in most cases induced massive eczematous reactions consisting in infiltration, reddening and vesiculation. Weaker dilutions almost invariably produced reddening and vesiculation without infiltration and the weakest dilutions which caused any response gave rise to scattered vesicles, but no reddening or infiltration. Usually a vesicular reaction was elicited by a much weaker concentration if teepol was added than if a purely aqueous solution was applied. Similarly the aqueous solution did not cause reaction in any case in which the one with teepol® had not induced vesicles. These results showed that addition

(4) J. Invest. Dermat. 26:421-426, May 1956.

reticuloendothelial tumors. It must be noted that in such tests preceding external applications of some drugs may inhibit both metabolic processes

Sections of the material tested by the above method were also studied histochemically particularly the formation of formazan i.e. reduction of triphenyl tetrazolium-chloride. It was seen that in the epidermis there are substances that are removed by watering or placing the sections in Ringer's solution their disappearance from the epidermis concurs with markedly blocked respiration reduced glycolysis and histochemically noted loss of formazan formation.

Intermediate Carbohydrate Metabolism of Epidermis II. Assay for Succinic Dehydrogenase and Cytochrome Oxidase. Robert D Griesemer and Edith Gould[3] (Harvard Med. School) used the homogenate method in analysis of rat epidermis for succinic dehydrogenase activity This is one of the most active epidermal respiratory enzymes and its activity is reflected by rate of oxygen utilization Only a few factors and one other enzyme, cytochrome oxidase, need be considered Succinate is oxidized to fumarate by succinic dehydrogenase and cytochrome C is reduced. Then cytochrome oxidase reoxidizes cytochrome C and simultaneously removes oxygen from the medium to yield water In assay of the two enzymes, the rate of oxygen disappearance is measured

METHOD —Oxygen uptake was measured by the Warburg apparatus. Homogenates of epidermis from the skin of white rats were prepared in distilled water after one minute of homogenization. Manometric experiments were conducted and the data plotted for the first 2½ hours. The rate of oxygen uptake during this period QO_2 (µl. O_2/hour/mg dry homogenate) was considered characteristic of the conditions studied. The assay method of Schneider and Potter was used for simultaneous determinations of succinic dehydrogenase and cytochrome oxidase.

The optimal concentrations of all factors in these enzyme reactions are given for homogenates of rat epidermis. Under optimal conditions, QO_2 of succinic dehydrogenase is 1.89±0 37 and QO_2 of cytochrome oxidase 12 5±1.8. Future studies correlating enzyme activities and functional and structural abnormalities may clarify the pathogenesis of disease.

(3) J Invest. Dermat. 25:383-389 December 1955.

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(?) J. Invest. Dermat. 26:421-426, May 1956.

of surface-active agents can disclose certain cases of allergy which standard tests cannot.

The more ready elicitation of an allergic reaction after addition of a surface active agent presumably results because the response becomes manifest when the allergen has penetrated sufficiently deep into the skin The toxic reaction however practically speaking is elicited by the same concentration regardless of any addition of surface active agent. This is probably because the toxic changes reflect denaturation of the skin proteins therefore further development of the process does not take place until the most superficial layers are saturated with reaction products

► [Teepol® is a secondary alkyl sulfate. The increased intensity of patch test responses from combinations of detergent and allergen makes one suspect that at least some of the hand eczemas which have been blamed solely or mainly on the action of the detergents themselves may actually be due to an enhancing effect of the detergent on an otherwise subthreshold exposure of allergen. The question remains regarding the mechanism by which teepol® exerts this action Is it by increasing penetration in quantity or depth, or is it by producing some thickening of the prickle cell layer which, as has been shown by Baer Rosenthal and Sims (J Invest. Dermat. 27:249 1956) in guinea pigs at least, increases the capacity to react with eczema like changes.—Eds.]

Water Content of Stratum Corneum III Effect of Previous Contact with Aqueous Solutions of Soaps and Detergents. Irvin H Blank and Elvera B Shappirio[5] (Harvard Med. School) discuss action of chemicals used in the manufacture of household soaps and detergents on that portion of skin which lies outside the barrier i e. the hydrophilic cornified epithelium

METHOD.—Materials used were sodium triphosphate, an alkyl sulfate an alkylbenzene sulfonate and a coconut oil soap. Calluses sanded to 0.3 mm. were dried and then maintained at constant humidity Each callus was placed in 25 ml water or a 1% solution of one of the materials for two hours at 40 C then washed and hung over concentrated sulfuric acid for two weeks to obtain a new dry weight.

After soaking in water or aqueous solutions of soaps or synthetic detergents thin sheets of callus are less flexible than before Soaking in water only slightly reduces the water holding capacity of cornified epithelium Soaking in soap solutions reduces the water holding capacity as much as does soaking in synthetic detergent solutions Reduction of water holding capacity is not measurably altered by the

(5) J Invest. Dermat 25:391-401 December 1955

addition of sodium triphosphate to either soap or synthetic detergent solutions. Water-soluble nitrogenous materials can be extracted from calluses or intact cornified epithelium by water alone or by aqueous solutions of soap or synthetic detergents. Soap solutions extract as much of these materials as do synthetic detergent solutions. In all of these extrac tives, th amount of aromatic amino acids appears relatively constant. Data reported here do not indicate that chemical commonly used i manufacture of household detergent alter cornified epithelium differently than does coconut oil soap. Acco ding to these investigations ynthetic detergents were found to be more damaging to skin than soap

Is pH Value Increased Everywhere on the Skin Surface of Eczema Patients? Previous investigator found that the pH values of non n ol ed skin areas were 0.17-0.25 pH (in the chest and fo earm regions respectively) h gher in ec ema patient than i control person without eczematous conditions. Since external nfluences e g wash ng with soap and therapeuti application of shake lotion, could not be e cluded there was no definit conclu ion as to whether the pH in crease of nonin ol ed areas of eczema patients was due to endogenous factors. To check on these findings, C G Schir ren and H Pawl w ky[4] (Uni of Mun ch) made pH deter minations on 50 eczema pat ent (with disseminated lesions of contact dermatiti hronic eczema ec ema paras tarium and so-called endogenous eczema) and 50 controls free from eczema. Determinations were made in 10 different noneczematou test areas of each exam nee (forehead, cheek neck houlder presternal region, antecub tal fossa, flexo and ex tensor urface of forearm, and medial and lateral aspect of leg). Ea h area was tested six times and the average value wa computed.

The pH alue of the entire integument was found to be from on -third to one-half higher n eczema patients than in those without eczema. External nfluences could be excluded, since th findings were the same in areas wh ch are u ually washed often such as the hands and face as in those which are seldom washed. Thi was true of pat ent w th recent un t eated eczematou condition nd in others who had been treated topically for some time. Som of the eczema patients

(4) Dermatologica 112 223-229 March, 1956.

stated that their skin had been "sensitive," particularly to soap before the eczematous changes occurred.

► [These findings confirm those in the preceding article and those of Schauwecker (Dermatologica 111 197 1955) —Eds.]

Electrometric Determinations of pH of Cutaneous Surface in Persons with Normal Skin and in Eczematous Patients, with Particular Reference to Acid Neutralization were carried out by R. Epprecht[7] (Zurich) Using an electrometric instrument for pH determination a new method was worked out for checking the acid neutralization of the skin.

METHOD.—To a dry circular area (diameter about 27 mm.) on the extensor surface of the forearm, 1 drop of 1/150 N sulfuric acid is dropped 10 times. The time is determined which is required for neutralization of each drop to a certain pH value. The pH determined after the 10th drop is used to classify the acid neutralization of the subject.

The acid binding capacity was found to be remarkably constant in persons with normal skin and was not correlated to pH values Sweat secretion accelerated the acid binding capacity In 35 patients with localized acute or chronic eczema (endogenous, seborrheic, microbial parasitic eczema or contact dermatitis) acid neutralization capacity and surface pH were unchanged in the test. In 16 patients with acute, generalized or very disseminated eczema surface pH was often increased and acid neutralization considerably accelerated.

Because of the marked shift of skin pH toward alkalosis the alkali and acid resistance of the skin were also tested. In these patients alkali neutralization was retarded alkali and acid resistance impaired With improvement of eczematous changes normalization of acid and alkali neutralization and also of pH values occurred after a few days or weeks It therefore seems that two types of retarded alkali neutralization exist. (1) The constitutional type shows normal pH values and normal acid neutralization in ichthyosis constitutionally retarded alkali and acid neutralization are present. (2) The second type has so far been observed only in extremely disseminated eczema here cutaneous pH is increased acid neutralization accelerated and acid and alkali resistance deteriorated. This type is only transitory normalization taking place together with improvement of eczematous changes. It is assumed that this temporary alkalosis is

(7) Dermatologica 111:204-223 October 1955.

due to poss'ble pathologic changes that occur in apparently normal skin, which cannot be ascertained clinicall)

▶ [It should be noted that clinically unaffected skin areas participate in the "alkalosis which the authors found in generalized eczema and that the alterations in pH persist for several weeks.—Eds]

Changes of pH, Alkali Resistance Alkali and Acid Neutralization of Skin after Various Baths were studied by Felix Laube[4] (Zurich) Complete baths (200 L. water at 35 C., for 15 minutes rinse with tap water for 2 minutes) were given with tap water only almond bran 100 Gm. sea salt, 3 kg Palmoli e soap, 20 Gm. Sinalca soap 20 Gm. (cons sts of lauryl-alcohol-sulfonates) and Vel, 40 Gm. (contains alkyl aryl sulfonate) Forearm baths were given in 10 L. water with soft soap 5 Gm. Emavon, 3 Gm. (purified osseous material and cellulose derivat es) and Serf 3 Gm (has a pH of 9.6 and consists of fat alcohol-sulfonates and various alka lis) Determination of pH was made electrometrically

Alkaline as well as neutral cleansing materials, part cularly those with marked degreasing effects change alkali resistance and alkali neutralization distinctly whereas pH increases only after use of alkaline cleansing materials. For instance, Serf increases the pH of the skin for a few hours by at least 2 units and also reduces alkali resistance considerably Soft soap has milar effects. Vel which is neutral, hardly changes pH but still damages alkali resistance and definitely delays alkali neutralization Vel possesses a marked surface tension and therefore ntense foam action, for which reason it is often used for foam baths.

Mild cleansing baths are those prepared with almond bran and with salt, both of which hardly change pH and alkali resistance and therefore are the least irritating Acid neutralization proved to be of minor importance After alkaline baths with Serf or soft soap acid neutralization is improved because the pH of the kin is changed toward the lkaline side. Baths with almond bran, Emavon tap water salt, materials which hardly alter the kin pH ha e scarcely any influence on acid neutralization. Clinical experience conformed to these findings

It s concluded that testing changes in pH and alkali resistance and neutralization is a useful method of evaluating kin tolerance to bath lotions and cleansing materials.

(4) Dermatologica 112 13-467 Apr June, 1956.

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(7) Dermatologica 111:204-223 October 1955.

Peter Flesch, Abraham Satanove and Crawford S. Brown[1] (Univ. of Pennsylvania) describe these methods as used on surgical and autopsy specimens. The extent of penetration can be ascertained by spot tests in the corium with reagents specific for a substance, by colorimetric assays of dermal extracts, or by chemical analysis of dermal sulfhydryl groups.

METHOD.—Skin from amputated legs, breasts and autopsy specimens is wiped with ether and cut in pieces ¼ sq. in. Test substances and controls (ointment bases) are uniformly applied for one to ten minutes. Subcutaneous fat is trimmed and a protective silicone cream applied to the undersurface of each piece, which is then incubated at 35 C. in tightly sealed jars. Samples are cut from incubated specimens, each surface is wiped with three changes of ether-soaked cotton pledgets and the epidermis is removed by the stretch method. Spot test reagents used on the corium are (1) dilute ferric chloride solution, giving a purple color with salicylic acid; (2) 25% antimony trichloride in chloroform, giving a rapidly fading blue color with vitamin A; (3) saturated alcoholic phenylhydrazine followed by N HCl, producing a reddish purple color with potassium bichromate; (4) 2% aminoantipyrine in 2% sodium carbonate followed by 2% potassium ferricyanide, giving a red color with phenolic compounds. Sulfhydryl groups are determined with 20% duponol, followed by Bennett's reagent. Direct colorimetric tests are done with dried extracts of corium in a salicylic acid-soluble solvent, using a photoelectric colorimeter.

Salicylic acid penetrated rapidly from plastibase hydrophilic plastibase, and lanolin. Carbowax® was less efficient and petrolatum was slowest in releasing salicylic acid. Sodium salicylate did not penetrate the epidermis from any of the bases tested. Vitamin A did not penetrate unless salicylic acid was added to the ointment. Phenol penetrated rapidly from all vehicles tested. On the basis of sulfhydryl inactivation, ammoniated mercury penetrated better from hydrophilic plastibase than from other bases tested. Sulfur decreased sulfhydryl concentration to the same degree, regardless of the base used. An excellent correlation was found between the penetrating ability and sulfhydryl inactivating capacity of potassium bichromate in two different ointments. In vitro studies of percutaneous penetration in dead skin compared favorably with in vivo studies provided the dead skin had been kept at refrigeration temperature from the time it was obtained until used. The in vitro tests are advantageous in that they are objective and do not rely on subjective clinical criteria.

(1) J. Invest. Dermat. 25: 289-300, November, 1955.

Permeation of Electrolytes through Skin. G Stuttgen and H Betzler* (*Med Academy of Dusseldorf*) *report the results of in vitro experiments with radioactive tagged* Ca^{++} SO_4^{--} and PO_4^{---} ions

METHOD.—Freshly dissected skin of mice and guinea pig was stripped of hair cleansed in Ringer s solution and mounted on glass tubes 2.5 cm. in diameter A large glass container was filled with 25 cc of Ringer s or saline solution and the glass tubes were immersed deep enough for the solution just to wet the membrane on the tube. The entire apparatus was then placed in an incubator and kept at 37 C. A constant amount of 2 cc of radioactive tagged solution was poured onto the membrane. During 24 hours (i.e duration of the experiment) 5 cc. was taken from the Ringer s solution five to eight times and the radioactivity determined by a Geiger counter Absolute values found were evaluated by a complicated formula.

The skin of the *mice and guinea pigs* showed a measurable permeability for calcium sulfate and phosphate ions. Permeation from cutis to epidermis was markedly higher than from epidermis to cutis In the calcium sulfate-phosphate series (i.e. in the series of bi and trivalent molecules) permeation values were lowered when permeation took place from epidermis to cutis but raised when it took place in the opposite direction Results showed that permeation may progress contrary to decreasing concentration and an increase of initial concentration causes increased percentile permeation values When before permeation experiments the animal skin was treated with 20% solutions of monoiodine acetate (pH 1 4 and 6.4 each for 1 hour) or 0 5% solution of mercury bichloride (for 1 hour) or was exposed to temperatures of 70 C (in container filled with water of 70 C for 10 seconds) and 0 C (for 4 hours) it was seen that monoiodine acetate mercury bichloride and exposure to temperatures of 0 C caused markedly increased permeability exposure to temperature of 70 C decreased it

On the basis of these results the authors hypothesize the existence of organizing factors which regulate the permeability of the skin.

► [Of course the question arises (it always does in animal experiments) to what extent, if any can the findings in hairy animals from which the hair has been stripped and the skin stretched over a glass tube be applied to man?—Eds.]

Laboratory Methods for Studying Percutaneous Absorption and Chemical Effects of Topical Agents on Human Skin.

( ) Arch. klin expert Dermat 203 472 482, 1 56.

Electrodermatogram and Its Use for Showing Pharmacologic Effects. The daily rhythm of the egetative nervous system, e., fluctuations of vegetative tonus duri g one day can be registered by determining the electric conductivity (or esistance to polarization) of the skin through which direct current is passing (electrodermatogram Regelsberger) Using the electrodermatogram (EDG) K. H Karcher[3] (Mannheim, Germany) studied changes of the daily vegeta tive hythm caused by drugs effective on the egetati e nervous system.

Method.—The set used for EDG determinations, manufactured by Siemens and Reiniger has highly sensitive ampere meter a ts olt battery and two gold covered, disk-shaped electrodes cov ered before use with gauze soaked in saline. Patients were put to rest in a room of constant temperature and were undressed before each EDG determination was made. Determinations wer carried out for 1½ hours on the anterior aspect of the body corresponding to 5th cervical (neck) 3d thoracic (thorax) 9th thoracic (abdomen and liver) 7th cervical (forearms) and 2d lumbar (thighs) segments After tw control determinations, the patients were given the substance to be tested and EDG determinations made on the same day or repeated after few days of continued treatment.

Altogether 1,032 determinations i 65 patients with venereal and cutaneous diseases and surgical d sorders (controls) were carried out. The influence of 12 groups of various drugs with different action on the neuro egetati e nervous system wa st died These included para ympathicomimetic and -lytics sympathicomimetics and -lytics electrolytes e.g calcium and magnesium hormones tamin A and seda t es effecti e n the brain tem e g phenobarbital and the erebral cort x.

The effect of the arious drugs were clearly evident in EDG curves. The para ympath colytic effects of atropine ympathicomimetic action of epi ephrine and agotonic h thm due t cholin citrat were demonstrated. In bronchial asthma and after local appl cation of heat the EDG urve wa unchanged In two cases of erythroderma medicamentosa the hythm wa uppressed but returned to normal w th the disappearanc of cutaneous changes, thus proving that egetative rhythms are nullified by inflammatory processes The rhythm w also supp essed after administration of narcotics effective on the brain stem or on the cerebral cortex and after admini tration of the central ympathico-

3) Arch klin. u. exper. Dermat. 203 454-471, 1956.

► [The in vitro tests may be entirely objective and devoid of the necessity of relying on the observer's clinical judgment, but no technic, no matter how refined, can undo the fact that they deal with dead skin! The poor showing of the carbowax base is striking, since one of the advantages of this synthetic material is claimed to be that it readily releases its active ingredients.—Eds.]

Quantitative Examinations on Cutaneous Absorption in Warm Blooded Animals with Radioactive Isotopes were carried out by H Kutzim[2] (Univ of Cologne) Percutaneous penetration of drugs is theoretically and clinically important and has been studied by many investigators Since methods used so far yield mainly qualitative information, a new method was experimentally worked out to determine absorption values quantitatively i e. the amount of absorption from topically applied ointments and oils per time unit.

METHOD.—Absorption values are determined directly with the aid of radioactive substances incorporated in ointments or oils.

Saddle-like cylinders (inner diameter 2.5 cm.) are molded from artificial material. The upper aperture of such a cylinder can be closed by a lid, and the lower rim has a horizontal extension with several perforations by which the cylinder can be fixed to the dorsum of a test animal or to the arm of a test person. After the test area is shaved, liquid cement phosphate is spread to the surrounding area and the cylinder firmly applied cement phosphate penetrates into the perforations of the cylinder and soon solidifies, fixing the cylinder firmly

For preparations of the radioactive ointment, 20 mg inactive sodium iodide is mixed in a small glass container (e.g watch glass) with 1/40-1/100 mc. of practically weightless NaI^{131} dissolved in water dried at 80 C in an incubator and finally mixed with 180 mg of ointment to be tested. This mixture (10 mg.) is applied either to small rubber plates placed on the shaved test area or rubbed into the test area with a rubber stopper

The test animal (rat) is tied to a small wooden board and placed on a rubber band suspended bridge which presses the cylinder into the hole of a lead plate, thus keeping the cylinder at a fixed distance from a Geiger Müller counter During the measuring period, about 2 minutes the animal becomes radioactive because of absorption the amount of radiation is determined by the counter

When I^{131} was used values were mostly below 2% Generally 10 animals were tested and average values dispersion and average inaccuracies of average values determined. The latter were found to be 1.83% for a count of 6,500/minute

With this method (used also in man) absorption of normal and of covered skin was studied in areas degreased by ether and in dermatitis due to cantharides The influence of various ointment bases was also tested.

(2) Arch. klin. u. exper Dermat. 203 137 141 1956.

within 24 hours of application of hydrocortisone-4-C^{1}. The peak of excretion of radioactive material was reached in the second 24 hours following which activity fell to relatively low levels by the fourth day and persisted essentially unchanged thereafter. Although precise quantitative data could not be determined, less than 1% of the topically applied radioactive steroid was excreted in the urine over a period of six days. The excretion pattern suggests that, after an initial relatively high excretion rate, a depot of hydrocortisone exists somewhere, perhaps in the skin, and that small amounts are steadily released for many days.

► [The question of percutaneous absorption of topically applied hydrocortisone is one that has caused much interest and concern. Previous studies by various investigators have failed to demonstrate any increase in blood or urinary *hydrocortisone* following inunction of hydrocortisone ointment onto the skin. The recovery of radioactivity in the form of tetrahydrocortisone (THE) and tetrahydrohydrocortisone (THF) (both of which are physiologically inert) does not yet prove that active hydrocortisone gets beyond the local skin site to which it is applied. It remains yet to be determined whether the hydrocortisone is converted to THE and THF while in the skin or after absorption into the body circulation. —Eds.]

Penetration and Distribution of C^{1} Hydrocortisone in Human Skin after Topical Application was studied with radioautography by Allene Scott and Frederick Kalz[5] (Royal Victoria Hosp., Montreal). Normal skin of the upper back was used to obtain biopsy specimens. A 1% hydrocortisone ointment was the carrier in all experiments. Radioactive hydrocortisone was mixed with the stable powder to give a concentration of 1 μc. C^{1} hydrocortisone/mg. of the stable form. A total of 50 mg. ointment was massaged into an area of 1 sq. in. Five mm. punch biopsy specimens were obtained and processed.

After one hour, radioactive material was seen in the epidermis and in two hours had concentrated in the basal layer. After 6 hours, C^{1} was identified in the cutis about blood vessels and had disappeared entirely from the skin after 16 hours. With hyperkeratotic, lichenified skin the material had not entered the epidermis by two hours but had after six, indicating that thickening much retarded penetration. Application of the tagged hormone to irradiated (grenz or ultraviolet) skin resulted in more rapid penetration before and during early erythema but was no different from normal in

(5) J. Invest. Dermat. 26 149-158, February 1956.

lytic reserpin. Administration of extracts of whole pituitary caused various changes in the EDG curves depending on the doses given A seborrheic patient with bacterial eczema and microbid showed marked clinical improvement and normalization of the EDG after vitamin A treatment (300,000 units three times/week intramuscularly plus 100 000 units/day orally) a harmonizing effect of vitamin A on the neurovegetative *nervous system was assumed. In patients with* neurodermatitis the EDG showed in control determinations sympathicotonic changes after administration of pituitary extracts clinical improvement and normal rhythm occurred, but with clinical relapses sympathicotonic EDG curves recurred.

The author emphasizes the clinical value of the EDG which is a comparatively simple but effective method of disclosing pharmacologic effects on the vegetative nervous system

► [These studies are based on two assumptions which as far as the editors can judge are unproved, namely (1) that there is a regular vegetative rhythm (the authors define this as a rhythmic change between dissimilation and assimilation) and (2) that the method of tracing the electrodermatogram is reliable.—Eds.]

Percutaneous Absorption of Hydrocortisone-4-C^{14} in Two Human Subjects has been investigated by Frederick D Malkinson and Edward H Ferguson[4] (Univ of Chicago) by applying the steroid in ointment form to normal human skin and *examining the 17 ketosteroid fraction of the urine* for radioactivity The beneficial anti inflammatory effects produced by hydrocortisone used topically suggest some absorption of this hormone into the skin but no direct evidence for this assumption has heretofore been presented.

METHOD.—Patient 1 was a woman, 41 with severe bullous dyshidrosis of the hands. Patient 2, a women, 58, had abdominal herpes zoster Hydrocortisone ointment 2.5% was applied to 39 sq cm. of normal skin over the flexor surface of the forearm Ointment, 59 mg containing 0 15 mg of C^{14}-labeled hydrocortisone was applied to patient 1 and 111 mg containing 0.28 mg of C^{14}-labeled hydrocortisone to patient 2. The sites were covered with a perforated aluminum eye patch taped to the skin. Daily 24 hour urine specimens were collected for six days, at which time the dressings were removed. The 17 ketosteroid fraction of the urine was isolated by the Koch method, modified by Landau. Disintegrations/minute were calculated for each total extract on a weight basis.

Significant radioactivity appeared in the urine of patient 1

(4) J Invest Dermat 25 281 283 November 1955.

Vaccinial Infection of Cornea, and Mitotic Flare-up from Palmitic Ointment are reported by E. Musso[7] (Univ of Geneva)

1. Experiments with cortisone. (*a*) Croton oil dermatitis in guinea pigs, produced by single pplication of oil to the flank, was not influenced by injections of cortisone (80 mg./kg./day) Sedimentation rate was no different in guinea pigs treated or not treated th cortisone. (*b*) Diluted diphtheria toxin (1 4) was injected intradermally into the flanks f 26 guinea pigs, 13 of which received subcutaneous injections of cortisone (80 mg./kg./day) into the other flank until the site of the Schick reaction was excised at 24 48, 7., 96, 120 and 144 hours after the toxin injection. Neither macro- nor microscopic differences were noted between animals treated with cortisone and control animals. ( ) In a patient, three round areas (diameter 7 cm.) on the left half of the back received ultra iolet irradiation for 15 25 and 35 seconds, respecti ely After 6, 12, 24 7? and 96 hours, the intensity f the erythema at each site as determined. In a second experiment, the same patient received cortisone injections, 100 mg twice day for 48 hours. The right half of the back was then exposed to ultraviolet ray and the intensities of erythema were determined as before Cortisone injections were continued throughout the experiment. Neither ppearance nor development of erythema was influenced by cortisone.

.. Experiments with hydrocortisone. ( ) Both corneas f tw rabbits were injured by scarification and fected with the liquid from esicles of herpes simplex labialis. One eye was treated w th 1 drop of 5% hydrocortisone acetate solution, pplied every 2 hours for 10 days. Similarly the corneas of tw rabbits were infected with undiluted (smallpox) vaccine and treated in the same ay N difference was observed in the development of either herpetic or accinal infection in treated and untreated corneas. (*b*) I four children, ultra iolet erythema, produced by exposure for 15 seconds to upper arms and for 25 seconds to forearms, was treated by application of 2.5% hydrocortisone ointment to one arm and ointment base to the other Dressings applied to irradiated areas were removed after 12, 24 48 and 72 hours to check amount f erythema. No difference of evolution and intensity f erythema was noted between area treated with hydrocortisone and those to which ointment base only was applied. (*c*) In four guinea pigs cetylic ointment (sic.—Eds.) was applied to the right and cetylic ointment containing 5% hydrocortisone to the left nipple. After 24 hours colchicine was injected into the guinea pig in order to block mitoses 9 hours later nipples were excised and examined histologically It was found that marked mitotic growth stimulated by cetylic ointment was not influenced by topical pplication of hydrocortisone

M so con l des from these experiments a d oth r negativ res lts with cortisone and hydrocortisone that preven

[7] Acta endocrinol. 21 77-83, January 956

late erythema The rate of penetration did not differ when other vehicles were used. Epidermal penetration of hydrocortisone and its temporary concentration in the basal layer of the epidermis were definitely demonstrated, and it is suggested that the basal layer is the center of metabolic activity Penetration of hydrocortisone through follicular structures was not confirmed

Reaction of Normal Human Skin to Intradermally Injected Hydrocortisone Histologic and Histochemical Study was conducted by William B Atkinson Raymond R. Suskind and Leon Goldman[6] (Univ of Cincinnati) Microscopic examination of biopsy specimens removed ½ 72 hours after intra dermal injection of hydrocortisone acetate revealed formation of a particulate mass of basophilic material at the injection site in 24 hours The lesion appeared to be partly desoxyribonucleic acid from nuclear debris of disintegrating dermal connective tissue cells and infiltrating leukocytes and partly precipitated acid mucopolysaccharide from dermal ground substance. Free sudanophilic lipid from breakdown of dermal cells, was also present Connective tissue fibers seemed unaffected during the observation period. Despite extensive morphologic damage there was minimal inflammatory reaction

It seems improbable that the basophilic masses in the skin lesions of patients given hydrocortisone intradermally are directly related to the beneficial action of the hormone This view is supported by the fact that, although cortisone alone induces similar basophilic masses in both normal and diseased skin it has little or no therapeutic effect. For the present at least it must be concluded that intradermally injected hydrocortisone produces local tissue damage while at the same time it ameliorates pre-existing disease by suppressing inflammatory reactivity of the dermal connective tissue

► [The changes which were noted after injections of hydrocortisone have to be carefully evaluated with due consideration for the high concentrations used—concentrations which are much different from the small amounts which might be found in the cutis after topical application in the form of ointment or lotion and the even smaller amounts after systemic administration.—Eds.]

Negative Results Observed during Experiments with Cortisone and Hydrocortisone In Croton Oil Dermatitis Schick Test, Ultraviolet Radiation Dermatitis, Herpes Simplex and

(6) A.M.A Arch. Path. 62 8-11, July 1956

thema was short-lived and was followed immediately by conspicuous pigmentation of the irradiated area. This protective action lasted only as long as the hormone therapy. The ultraviolet reaction is probably largely due to liberation of inflammation producing substances in the damaged epidermis. Whether the diminished response to radiation is due to nonspecific depression by cortisone of the vascular component of the acute reaction or to a protective action on the epidermal cells is unknown.

► [This article is one of a number which have appeared during the past year in a new and promising field of experimental investigation. Animals which have received usually fatal doses of whole body irradiation shortly thereafter are given parenteral injection of bone marrow, spleen or other suitable cellular material from healthy isologous, homologous or heterologous animals. The cells from these nonirradiated donor animals then repopulate the heavily damaged blood-forming and other tissues of the irradiated animals, thus enabling them to survive an otherwise fatal dose of radiation. Animals which have survived in this manner then may show immunologic traits which are characteristic of those found in the donor animals. One example of their changed immunologic status is that they now will accept homografts or even heterografts from the donor animals which they would be expected to reject, unless they had previously been subjected to the radiation and cell injection procedure.—Eds.]

Effects of Chloroquine on Erythematous Reaction to Phenol in Patients with Chronic Lupus Erythematosus. Aldo Leoni[9] (Univ. of Padua) studied the reaction to phenol, with respect to latency and erythema intensity, before, during and after prolonged chloroquine treatment in nine patients with chronic lupus erythematosus. The reaction to phenol, as determined with Wedroff's test, was modified by chloroquine therapy and was characterized by an increased latency period and less intense erythema. Correlation between the modifications of the erythematous reaction and clinical improvement of the lesions was not constant or parallel. Weakening of the reaction was generally slow and progressive and became clinically *evident after two to four* weeks of treatment, whereas improvement in the lesions appeared early, sometimes after one week of treatment. In one patient in whom the reaction to phenol remained unchanged, the skin lesions were not improved by treatment. Chloroquine seemed to have a generic anti-inflammatory action which was partly expressed by an increased tolerance to light.

Administration of 1 Gm. chloroquine to patients with chronic lupus erythematosus and to controls indicated that

(9) Minerva dermat. 29: 478-411, December, 1954.

tion of inflammation or mitotic growth cannot be attributed to the drugs except in certain cases and under certain conditions

► [It is important to realize that the results of animal studies do not necessarily apply to man. For example, in man the local use of cortisone or hydrocortisone in the eye is contraindicated in the presence of a herpes simplex infection of the cornea (dendritic ulcer)

The findings that topical application of hydrocortisone *after* ultraviolet irradiation does not significantly change the resulting erythema is in agreement with the experience of Norman Kanof at the New York Skin and Cancer Unit. It is interesting to note that even systemic administration of cortisone, in the doses used, does not change erythema due to ultraviolet irradiation.—Eds.]

Effect of Cortisone on Skin Reactions to Local Histamine and Ultraviolet Irradiation was investigated by G Holti[8] (Univ of Birmingham) The effect of cortisone on the skin's triple response to local introduction of histamine was assessed by skin temperature measurements and observations of wheal and flare size Studies were conducted on two normal subjects and on three patients receiving cortisone for conditions not affecting their skin The triple response to histamine was produced by pricking histamine solutions into the skin daily for two days before cortisone was taken and every day during administration of the hormone and after it was discontinued until the vascular responses returned consistently to their precortisone level Three wheals of histamine 1 30 and histamine 1 300 were laid down in two parallel rows on the forearm in most tests Cortisone was given by mouth 100 mg daily for three to five days (taken for two separate courses) and 300 mg daily for one and two days (two separate courses) Eosinophil counts were made daily during each experiment

Cortisone diminished size of wheals and flares and increase in wheal temperature. Observations on wheal size and temperature were clear but the effect of cortisone on flare size, though statistically significant, was less obvious mainly due to wide personal variation of reflex flares even during steady states These changes are considered due to an effect on minute blood vessels

Cortisone greatly reduced intensity and duration of skin reaction to ultraviolet radiation This agreed with earlier reports that during cortisone administration the minimal erythema dose of ultraviolet radiation was doubled that ery

(8) Clin. Sc. 15:41 53, February 1956.

and the eosinophil count only slightl) The action of chloroquine on the diffusion power of the skin is not so clearcut and constant as that of cortisone The hypothesis of a cortisone-like action of the drug is denied because of the negative esults with Thorn s test in cases in which chloroquine did inhibit skin diffusion. Probably chloroquine exerts its i hibiting effect directly on the substratum with action analogou t that of acet) lcholine.

Effect of Topical Application of Corticotropin, Hydrocortisone and Fluorocortisone on Process of Cutaneous Inflammation was studied b) Allene Scott and Frederick Kalz[3] (McG ll Un) Mu tard o l and nitric acid were u ed as primary irritants, with erythema inducing doses of ultra violet rays

The authors found that effective inhibition of nflamma tio resulted from appl cation of hormone two to eight hours before the t mulus. The maximal effect was achieved in about hours A t me interval o er 16 hours failed to produce an effect. The minimal effective contact time of hormone with skin was one hour A contact time o er two hours did not increase the effect. The established minimal t me period of contact of hormone w th skin was thought to be related to the t me necessary for penetration of the hormone through sk This xplanation was supported by autoradiography The tim limits for demonstration of the effects of th hormones wa thought to suggest a later destruction or loss of the hormo es from th ti sues tested Opt mal and about qual ffect were seen w th concentrations of 1% hydrocortison 0 25% fluorocortisone and 5% cort cotropin Th re was an erse relationsh p between the intensity of the t mulus and the degree of inhibition observed in the in flammat ry espon e and betw een the thicknes of epiderm s term f cell layer and the hormonal ffect

If h rmones wer pplied under opt mal conditions, complete h bition of inflammation induced b) primary rritants wa observed in 75 of patients using hydrocortisone and fluorocortisone and n 60% u ing ACTH In 50% exposed to erythema nducing doses of ultra iolet radiation a reaction failed t d elop if pretreated with these same hormones.

It bel eved that these hormones can nhibit inflamma

3 [illegible] Dermat 24 341 373, May 1956

the degree of weakening of the erythematous reaction to phenol was in both groups in direct proportion to the concentration of drug in the body This effect was maximal 1 1½ hours after ingestion of the drug remained at this level 1 2 hours and returned to the initial state after 2 3 hours. The early improvement in the lesion with respect to the late modifications of the erythematous reaction can probably be explained by the fact that there is a greater accumulation of the drug in the lesions.

► [These findings are in consonance with those of previous investigators. Apparently chloroquine has an anti inflammatory effect which is demonstrable in subjects with and without lupus erythematosus and which reduces the skin reaction to phenol. For example, the findings of Bluch and Gerlach (Hautarzt 6.267 1955) in mice were interpreted as demonstrating that chloroquine has a marked antiphlogistic effect on artificially produced cutaneous inflammation.

Temime (Bull. Soc. franç. dermat. et syph., pp. 473-475, Nov Dec., 1954) demonstrated that compounds in this group interfere with the prothrombin system. Cahn Levy and Shaffer (see this YEAR BOOK, p. 6) found that chloroquine modifies certain abnormal but not the normal responses of human skin to ultraviolet light in the sunburn spectrum.—Eds.]

Experiments on Mechanism of Action of Chloroquine Action of Chloroquine on Phenomena of Diffusion was studied in 23 patients with various dermatitides by Aldo Leoni, Gianbattista Marson and Carlo Rossetti[1] (Univ of Padua) The hypothesis of a cortisone or corticotropin like action of the drug was tested at the same time in 15 patients with the Thorn test Evans blue (0 05 cc.) with a solution of hyaluronidase (0 05 cc) was injected intradermally in the patients backs and the first eosinophil count made. The area of diffusion was measured by tracing its edge on cellophane after 1 and 2 hours in 11 patients and because of insignificant differences in the two readings after 1½ hours in the others At the same time 2 tablets of chloroquine were given Three hours later when the chloroquine blood concentration was highest the injection was repeated and the diffusion area measured the same way and at the same time intervals as before. Four hours later the eosinophil count was repeated

The skin power of diffusion was diminished, in varying degrees, in 16 patients and increased in the other the eosinophil count was decreased in 13 and definitely increased in 2 In the one patient with scleritis who recovered quickly with chloroquine, the diffusion power was decreased notably

(1) Minerva dermat. 31:261 263, Septembe 1956.

and the eosinophil count only slightly The action of chloroquine on the diffusion power of the skin is not so clearcut and constant as that of cortisone. The hypothesis of a cortisone-like ction of the drug is denied because of the negati e results with Thorn s test in cases in which chloroquine did inhibit skin diffusion. Probably chloroquine exerts its hibiting effect directly on the substratum with action analogous to that of acetylcholine.

Effect of Topical Application of Corticotropin, Hydrocortisone and Fluorocortisone on Process of Cutaneous Inflammation was studied by Allene Scott and Frederick Kalz[2] (McGill Uni) Mustard oil and nitric acid were used as primary irritants with erythema-inducing doses of ultra violet rays

The author found that effecti e inhibition of inflammation resulted from application of hormone two to eight hours befor the stimulus. The maximal effect was achieved in about si hours. A time nterval o er 16 hours failed to produce any ffect The minimal effective contact time of hormone w th skin was one hou A contact time over two hours did not increase the effect. The established minimal time period of contact of hormone with skin was thought to be related to the time necessary for penetration of the hormone through skin Thi explanation was upported by autoradiography The time limits for demo stration of the effects of the hormones wa thought to suggest later destruction or loss of the hormo es from the tis ues tested Optimal and about equal effect were seen with concentration of 1% hydrocort sone 0 25% fluorocortison and 5% corticotrop There was n in erse relationsh p betw een the intensity of the stimulus and the degree of inh b tion observed in the in flammat ry esponse d between the thi knes of epiderm s in term of cell layers and th hormon l ffect

ll hormones were pplied under optimal cond tions complet inh bition f nflammation nduced by primary irritants wa bserved in 75% of patients u ng hydrocortisone and fluorocortisone and 60% u ing ACTH In 50% exposed to erythema-induci g doses f ultra iolet radiation, a reaction failed t dev lop f pretreated w th these same hormones.

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[2] J Invest Dermat 24 361 378, May 1954

tion provided that they are present in adequate concentration in the tissues at the time of application of the inflammatory stimulus It is also thought that the hormones inhibit the reaction of the cells to the primary products of inflammation

Comparable results were noted with corticotropin. This appears to be due to an extra adrenal effect of the tropic hormone. Possibly corticotropin acts directly on the target cells in its primary biochemical role.

► [The activity of corticotropin locally applied in these experiments is unexplained. Lorincz, in discussing this paper suggested that this may be due to the vasoconstrictor action of pitressin* contained in the corticotropin. It is difficult to interpret the autoradiographs in the original article without knowing more regarding their preparation.—Eds.]

Pathogenesis of Urticarial Inflammatory Pruritus.—*III Quantitative analysis of drugs controlling local pruritus induced by morphine*—Preliminary investigations revealed that local itching caused by morphine can be inhibited by drugs which have anti inflammatory effects or interrupt the reflex arc, either peripherally or centrally also that inflammatory exudation does not always cause urticarial inflammatory pruritus because itching may develop despite completely stopped circulation In the present study E. Rajka S Korossy and Marianne Gózony[3] (Budapest) report extensive investigations of drugs which act on local itching caused by morphine.

METHOD.—A mixture was prepared containing equal parts of the usual parenteral dose of the test substance and of morphine solution the morphine content corresponding to the amount of morphine required for elicitation of itching (about 0.1 1.0 μg) 0.05 ml. of this mixture was injected intracutaneously into the forearm. When pruritus was inhibited by the test drug the concentration of the latter was reduced progressively ½ 1/3, 1/10 1/100 etc. until the threshold of inhibition of morphine-induced pruritus was found.

Experiments (3 098) with 78 drugs were made in healthy persons and in patients with various dermatoses Results of those experiments in which the inhibition ratio was at least 50% or more revealed that morphine pruritus was inhibited nearly completely in four fifths of the patients by calcium gluconate, in three fourths by glanduitrin [sic.—Eds.] trasentine * calcibronat and calcium chloride in two thirds by 19 drugs (ephedrine, gynergen TEAB [sic —Eds] scopolamine chlorpromazine antistine * neo-antergan * phener

(3) Dermatologica 112:81 107 February 1956.

gan,* multergan, Sandosten-Ca, procaine, stovaine, calcium bromide ammonium bromide, potassium bromide, magnesium sulfate, vitamin K, nicotinic acid and caffeine and in one half by 20 drugs (epinephrine, sympatol,* dihydroergotamine, yohimbine, eserine, atropine, novatropine regitine,* priscoline synopen, percaine, eucaine, calcium Sandoz sodium bromide, sodium silicate, vitamin B_1 B_2, B_6 and C, and nicotinamide) In most cases, experimentally produced pruritus could be inhibited by 44 of the 78 drugs. However it cannot be inferred that any one of these drugs in the usual dosage would inhibit itching in all cases

IV Contributions to theory of two-phase itching mechanism comparison with other skin axon reflexes—Rajka reports further experiments on the axon reflex nature of the first phase of the pruritus mechanism and on the analogy between it and other (vasodilator and sudo- and pilomotor) cutaneous axon reflexes. Experiments in which the binding-off method of Wada (superficial ligature of a limb by a small rubber band and intracutaneous injection of test substance on one side of the rubber band) was used, revealed that pruritus like the vasodilatory reflex (both elicited by urticariogenic substances, e.g morphine) and sudo- and pilomotor reflexes (produced by nicotinic acid salts) appeared after a latent period on the other side of the ligature, although the swelling of the intracutaneous injection remained limited to the side of administration. This phenomenon proves the axon reflex nature of pruritus. Furthermore, the itching reflex, like other cutaneous reflexes can be influenced by drugs which are effective on the receptor and effector point, i.e., on the receptor apparatus of the afferent and terminal apparatus of the efferent part of the axon reflex respectively

For testing the receptor point, a mixture of the test substance and drugs causing itching, vasodilation of the reflex area, sweating and piloerection, respectively was injected on one side of the Wada ligature. To observe the effector action, the substance to be tested was administered on one side and later the axon reflex-producing drug on the other side of the ligature

Tests done in this way with various drugs, particularly those influencing the vegetative nervous system, showed

) Dermatologica 12 189 225, March, 1956

tion provided that they are present in adequate concentration in the tissues at the time of application of the inflammatory stimulus It is also thought that the hormones inhibit the reaction of the cells to the primary products of inflammation

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(1) Dermatologica 112 81 107 February 1956.

taped areas as revealed by local epinephrine injection Three of the subjects had clinical hidradenitis suppurativa, which was also diagnosed histologically Microscopically keratinous plugging of the apocrine sweat duct (Fig 61) dilatation of the duct and severe inflammatory changes limited to one apocrine sweat gland unit we e seen. The adjacent glands hair follicles, sebaceous glands and deeper eccrine



Fig —Arrows point to keratin plug in apocrine pore and to dilated apocrine duct showing polymorphonuclear leukocyte infiltrate. There is evidence of recent rupture and secondary bacterial infection, ruptured above [illegible] 165 (Courtesy of Shelley W B and Cahn, M M A M A. Arch. Dermat. 72 562 565, December 1955)

gland were all normal. The tender deep nodules seen cl nically were an inflammatory hange in the apocrine gland only The pathogenes of the experimentally produced condition s follows The adhesi e tape leads to maceration, producing a keratotic plug in the apocrine duct orifice. The normal urface bacteria, trapped beneath the plug grow on the pocrine weat Polymorph nuclear leukocytes enter the duct and gland causing a local purulent reaction. It is oncluded that in h draden tis uppurati a there is occlusion of the apopilosebaceous orifice w th secondary bacterial infection of the apocrine gland, on whose organic material the

that itching could be inhibited by antipruritics in the receptor as well as in the effector area although more easily in the former where procaine antihistamines sympatholytics and parasympatholytics and calcium were effective The vasodilatory reflex (reflex hyperemia) generally assumed to be due to arteriolar dilatation by acetylcholine was inhibited mainly by parasympatholytics and synapsis blocking substances, local anesthetics and antihistamines whereas sympatholytics were somewhat ineffective. The pilomotor reflex (piloerection) was inhibited in the receptor area by nearly all substances tested but in the effector area only a few of these drugs were effective In the cholinergic sudomotor axon reflex the counterpart of the adrenergic pilomotor axon reflex drugs with more or less completely inhibiting effects on the receptor point were less effective or ineffective in the effector area

The facts that receptor areas generally respond better to various preparations than effector areas, that tests done in the same person with the same substance do not always reveal parallel effects on different axon reflexes and that various axon reflexes show differences in latent period, duration and time lapse until maximal action is reached all point to the existence of various nerve fibers and peripheral nerve cells of ganglionic cell character which form a joint terminal nerve reticulum Formation of various axon reflexes with variations in latent period spread and action can best be explained by the assumption of a vegetative terminal network, the ganglionic cell like elements of which would further explain the transfer of stimulus Hypothetically the latter occurs in the lower corium

Pathogenesis of Hidradenitis Suppurativa in Man Experimental and Histologic Observations of lesions of less than seven days duration are reported by Walter B Shelley and Milton M Cahn[5] (Univ of Pennsylvania) A perforated belladonna adhesive tape was applied to one axilla of 12 normal male adult subjects aged 20–40 The other axilla was the control site After one week biopsies were performed from each axilla serially sectioned and stained with hematoxylin eosin

In every subject apocrine anhidrosis developed in the

(5) A.M.A. Arch. Dermat. 72 562 565 December 1955

to 0.25 cc. sterile saline in a microculture tube. In the second method, apocrine sweat, collected under the same conditions was left in capillary tubes, and small amounts of culture suspensions in saline were allowed to flow into the tubes. All tubes were incubated at 37 C.

Results showed that sterile apocrine sweat remains odorless, even on incubation for several days. The introduction of appropriate bacteria will produce the *typical odor* within 24 hours and it does not appreciably increase after this time. A variety of species may produce odor; the odor produced by different species was identical. Many of the isolates of the resident organisms, mainly the diphtheroids and to a lesser extent the coagulase-negative micrococci, generated odor. Perhaps strains of the same species differ in this respect.

The apocrine gland, unlike the eccrine gland, empties into the pilosebaceous apparatus, and samples collected at the surface may be contaminated with minute amounts of sebum. Therefore sebum collected from another source (scalp hair) was added in appropriate dilutions to sterile saline, and specimens were inoculated with a known odor producer. No odor resulted in any of the tubes. Viable organisms were recovered on termination of the experiment, ruling out a bacteriostatic effect of the sebum.

In choosing agents to suppress bacterial multiplication the diversity of species which produce odor is significant. While the dominant species are gram-positive residents, wide spectrum antibiotics appear to have the greatest advantage since gram-negative organisms may also produce odor.

► (In the United States, at least, the sale of so-called germicidal soaps has increased tremendously at the expense of the regular toilet soaps. The most widely used germicidal soaps contain tetramethylthiuram disulfide or hexachlorophene. While these soaps may not be the complete answer to the problem of reducing sweat odors, it appears likely that their vastly increased popularity is in great measure due to this deodorant action. —Eds.)

Origin of Sebum is discussed by I. S. Hodgson-Jones. Whether the fatty substance on the skin surface is produced by sebaceous glands alone or is contributed from other sources has been controversial. The chief difficulty has been to separate products of sebaceous glands and sweat glands once they have been discharged on the skin surface. It has been stated that there are three possible sources of skin fat

T. St John Hosp Dermat Soc pp 26-30, Summer 1954

bacteria flourish. All clinical signs are the result of the deep apocrine infection with secondary inflammatory changes.

Fox Fordyce Disease **Histopathologic and Histochemical Investigation** was conducted by Richard K. Winkelmann and Hamilton Montgomery[6] (Mayo Clinic and Found.) on four patients who had axillary biopsy Histologic examination showed a basophilic material in the lumen of the involved apocrine glands, chiefly in the secretory portion. It was never observed in glands that had not undergone a great degree of atrophy of the cells and the gland wall. This material was found also free in the tissues, especially about the appendages The material is periodic acid Schiff positive diastase resistant and nonmetachromatic. It is sudan black B negative, resists extraction with hot pyridine and is probably a neutral mucopolysaccaride or mucoprotein.

The strongest argument for the importance of mucinous change in the glands as the starting point for the pathologic process is that it has been possible to see apparently normal and mucin-containing apocrine glands side by side in the dermis and even leading into the same follicle. The mucinous changes and the presence of mucin in the tissues may account for the exquisite pruritus.

► [The suggestion by the authors that the presence of mucin in the tissues may account for the pruritus would require further explanation if one considers that neither localized myxedema nor lichen myxedematosus are pruritic and both also contain mucin.—Eds.]

Bacteria Responsible for Apocrine Odor It has been shown that apocrine sweat is nonodorous when delivered to the surface but develops odor when acted on by cutaneous microflora The correctness of this view is demonstrated by the effectiveness of locally applied antibacterial agents to suppress the pungent axillary odor To identify the bacteria responsible for the odor John S Strauss and Albert M Kligman[7] (Univ of Pennsylvania) took cultures by swabbing the axillae of persons who had not used deodorants for some time Apocrine sweat was obtained after local stimulation by the methods of Shelley and Hurley

Cultures of the axillae yielded coagulase negative micrococci and diphtheroids in about 90% and 60%

Two methods were used In the first a capillary tube of apocrine sweat, collected under aseptic conditions was added

(6) A.M.A. Arch. Dermat. 74 63-68, July 1956.
(7) J Invest. Dermat. 27 67 70 August, 1956.

mechanical barrier to passage of sweat and sebum from the area bearing sebaceous glands to the center of the palm. When the cup was in place, despite profuse sweating no fat returned to the center of the palm.

* [Hermann and Prose (J Invest. Dermat. 16:217 1951) likewise excluding all extraneous sources of contamination, brought what the editors believe is excellent evidence that sebum is found on the palms.—Eds.]

Vater Pacinian Corpuscle in Skin of Human Finger Tip has been intensively studied and reappraised by Richard K. Winkelmann and Lamar S. Osment* (Med. College of Alabama). Recent work on the corpuscle in the prepuce of the newborn has shown it to be complex, coiled or arcuate rather than conforming to the classic description of a simple oval mass, consisting of concentric lamellae within which a nerve passes directly from pole to pole ending in a knob-shaped mass.

Method.—A piece of normal, adult human skin, from the volar surface of the tip of the index finger was fixed in 10% Formalin solution and embedded in paraffin; the sections, 10 μ thick, were stained with strong protein silver. Wax reconstructions were made of total corpuscles by projection of individual sections at known magnifications and by tracing this projection on wax, 2 mm. in thickness. When the wax plates were assembled in sequence, they represented a scale model of the body of the corpuscle, enlarged 200 times.

I[n] the surface [a]rea studied 18 complete Vater pacinian corpuscle[s] were found, in the equi[v]alent of 120/cc. of tissue. The bodies varied from 0.21 to 0.89 mm. in length and from 0.1[1] t[o] 0.80 mm. [i]n width. The average length wa[s] 0.51 mm. and the [av]erage width 0.44 mm. The bodies located su[-]perficiall[y] at the j[u]nction of th[e] derm[is] [a]nd [s]ubcutaneous t[issue] [were s]haped like a flattened sphere. Those found deep in the [s]ubcut[a]neou[s] tissue near large nerve trunks or large [v]essel[s] tak[e] more unusual [s]hapes—triangular, C-shaped, S-shaped [o]r comple[x] co[i]led forms. In these there is a con[v]oluted [s]talk through wh[i]ch the nerve passes to reach the main portion [o]f the body. The external form of the V[a]ter pacinian c[o]rpuscle may be determ[i]ned principally by physical fact[o]r[s] external to i[t]. Th[e] liquid filled body takes the best form that the developing t[i]ssue [a]round [i]t will permit. The re[su]lt[s] indicate, in general, that more corpuscles can be found by microscopic study than by dissecti[o]n.

Response of Human Eccrine Sweat Duct to Dermal Injury was [inv]estigated by W[a]lter C. Lob[i]tz, Jr., John B

* A.M.A. Arch. Dermat. 73:116-12[?], February 1956.

sebaceous glands sweat glands and epidermal cells, and it has been argued that epidermal cells are unlikely to contribute significant amounts of fat even when exfoliation is more rapid than normal

The problem is whether sweat glands contribute appreciable quantities of fat to the skin surface Because of the absence of sebaceous glands from the palms they lend themselves to investigation of this problem If all fat is cleaned from the palms and accidental contamination avoided then if sweat glands produce fat fat will reappear on the palms and the more sweating the greater the quantity of fat that will appear

METHOD—Hands and feet were cleaned with soap and water then with acetone and finally with carbon tetrachloride, so that all traces of fat were removed. An initial estimate of the fat was made to insure that the sites to be investigated were entirely fat free At varying intervals, further samples were taken to detect any return of fat. These investigations were made under conditions influencing the amount of sweating To inhibit sweating the subject was placed in a cool room inadequately clothed, with the feet in cold water baths. To induce sweating the subject was violently exercised while excessively clothed in a hot room and the feet were placed in a water bath as hot as the subject could tolerate

Fat only reappeared on the palms and soles when the subject was sweating profusely so an attempt was made to establish a quantitative relation between the sweat and the fat. The relation was not at all straightforward and there was no evidence that the amount of fat was proportional to the degree of sweating although without sweating no fat would appear

Any information about the chemical properties of this fat which appeared during sweating would be useful to establish its origin The iodine number of that fat was therefore estimated It was found to be the same as that of the fat on the dorsum of the hand and it was felt that the fats were probably identical The most likely explanation was that sweating facilitates fat seepage probably as an emulsion, over the palm or sole This would explain the absence of fat where there was no sweating

To prevent seepage of emulsified fat an aluminum cup was designed to cover the palm fitting firmly along its edge but leaving the maximum possible skin area available for testing in the center of the palm The cup was held in place by elastic strips over the back of the hand. This produced a

of Pennsylvania) froze a circular area about 2 in. in diam eter on the cheeks of five Negro males and nine white males for one to eight minutes, using Kurtin s technic. The longest period produced no more inflammation and required no more time for healing than the shortest. Maximal response was reached in one minute, and thereafter no further physiologic changes ensued with continued freezing Within 24 hours, all patients showed an area of superficial inflamma tion topped by a thin-walled bulla, which quickly ruptured. Healing was complete in one week.

Studying healing after planing at different depths the au thors observed that tissue removal as deep as 2.5 mm. was followed by uneventful healing, though there were a greater amount f inflammatory reaction more postoperative dis comfort and a longer heal ng time than with more superficial planing The average acne pit was 1 mm. or less deep some were 2 mm. deep It was found that hypertrophic scars may follow dermabrasion in predisposed subjects.

The deep acne scar is a highly irregular depression in the skin lined by keratin-forming squamous epithelium It oc casionally s completely filled with keratinous material. Squamous epithel um appears to be in a state of unrest, with festooning purs, tongues and ribbon of epithel um project ing into the corium At pla es, the epithelium is differenti ated into nests of seba eous cells, and occasionally a func tioning sebaceous gland empties its contents into the bottom of the pit Uncommonly ellus hair follicle opens into the pit, presumably ha ing been differentiated from the lining squamous epithelium in the same manner as the sebaceous glands The restless ep thel um may send out heets of cells which fuse with epithelial projections from adjacent p ts or from d fferent portions of the same pit, thereby forming a network of epithelial strands

After dermabrasion, portion of hair follicles, sebaceous glands, sweat gla ds and deep strand of epithel um from the pit remain and it from ll of these epithelial reser oirs that regeneration of the epidermi occurs (Fig 62) In fi e days the epidermal coveri g consisting of se eral cell layers, almost complet ly cover the defect In nine days, a stratified squamous epith l um covers the entire wound. At this time there st ll some parakeratosis but in three

Holyoke and Doris Brophy[1] (Dartmouth Med School) In a previous study of injury to human skin in which the entire epidermis was removed the following stages of repair of the eccrine sweat duct were noted (1) degeneration and preparation of the environment for the regeneration to follow (2) active cell migration and proliferation and (3) reorganization and orientation In the present study a single cut with a thin knife was made approximately across the middle dermis. This injury completely or partially severed the eccrine sweat duct but left the overlying dermis intact

It was found again that the human eccrine sweat duct has an inherent ability to play a role in epidermal repair Regardless of the type or location of trauma the sweat duct responds immediately at the site of injury by spiralling its lumen and surrounding this spiral with new epidermal prickle cells Such a response seems to be a consistent reaction of the sweat duct to guarantee its own position and mature configuration in any potential epidermal structure. This ability to respond is inherent within the duct and is not dependent on any neighboring epidermis

Such an intrinsic drive to maintain the structure and continuity of lumen to the surface of the skin is so fundamental that this response occurs first, regardless of the site of injury and of rationale of the response to the total damage It is only after this response has proved unnecessary that the long period of reorientation is undertaken so as to leave the repaired skin with as little abnormality as possible

This is accomplished in the superficial portion of the duct. However the deep portion is still a part of the total secreting unit and stubbornly keeps its spirals

► [The capacity of the highly differentiated components of the human epidermis to dedifferentiate for epidermal repair is remarkabl and is of the greatest practical significance. During World Wa II, S lzberger Kanof and the senior editor (Ann Surg 125 418, 1947) observed regeneration of the epidermis from intact epithelial elements (usually pilosebaceous at times sweat glands?) in deliberat ly produced deep chemical and thermal burns. It is probably the capacity of these epidermal remnants to re-epithelize denuded skin which prevent the occurrence of serious consequences in cases in which dermal abrasion or planing treatment i done very deeply —Eds.]

Acne Observations on Dermabrasion and Anatomy of Acne Pit. John S Strauss and Albert M Kligman[2] (Univ

(1) J Invest. Dermat. 26:247 262, April, 1956
(2) A M.A. Arch. Dermat. 74 397-404 October 1956.

The phenomenon was disco ered incidentally in five Negro adults on each of whom a 2 in. circular facial area was planed to an approximately deptl of 2 mm which is about halfway through the cori m of the facial skin The planed areas were on the cheek where vellus hairs predominate and coarse terminal hairs are sparse. Biopsy specimens were taken im mediately after planing n four of the fi e subjects, and in none was there evidence of remnants of any portion of the ellus hair or its follicle Regeneration of vellus hairs be came evident in two weeks, when downgrowths of epithelial cords had budded off from the basilar portion of the restored epidermis. These cords were for the mo t part cylindric but more irregular than fetal hair germs and often flaring at the base into imperfect club-shaped structures. It was not possible to demonstrate in connection with these putative hair germs the invariable presence of papillae, partly perhaps be cause not all wer reall go ng n to form hair follicles. Un less the papillae were already partly enclosed by the end of the epithelial downgrowths they were impossible to ident fy with certainty Generally such invaginated papillae could not be recognized before the third week. The earlier speci mens showed downgrowths apparently without papillae By three weeks no true differentiation into hairs or seba ceous gland wa yet appare t The four week pecimens were most evealing for the formation of new vellus fol licles was not ccomplished s multaneously nd thus differ ent tages f differentiation w re discern ble Hai clearly w s being ynthesized by some vellus follicles, but for the most part had not erupted through the skin as yet In the two month specimen many perfectly normal ellus hair follicles w th accompa y ng sebaceous gland were present. All wer in an acti e growi g phase. It is felt that despite some morphologic d fferences, th formation of vellus hairs f om dult ep dermi recapitulated the embryonal pattern.

► [W onder about the necessity or advisability of using the apparently newly coined ord "apopilosebaceous to replace the older and better descriptive term apocrine-pilosebaceous. —Eds]

Histology of Human Ear Canal with Special Reference to Ceruminous Gland is described by Eldon T Perry and Walter B Shelley (Uni of Pen yl ia) Cerumen produced by appendages of ear k coat the wall of the canal to gi e a tacky urface which traps nsect and foreign bodies which

( ) J Invest. Dermat. 25 439 1 December 1955.

weeks the epidermis appears normal. Although healing is complete by histologic standards at nine days, a much longer period is necessary for clinical healing as evidenced by fall-



Fig. 6.—Regeneration of epithelium from eccrine sweat duct 6 days after dermabrasion. Eccrine duct is forming new spiral in manner classically described by Lobitz and associates. Abraded surface is practically covered with complete epithelial covering; reduced from × 240. (Courtesy of Straus, J. S., and Kligman, A. M.: A.M.A. Arch. Dermat. 74:397-404, October, 1956.)

ing off of the crust and return of the skin to a normal color.

► [As has been pointed out in the abstract preceding this one, it is fortunate that components of the cutaneous appendages are capable of dedifferentiating and thus furnishing the epithelial covering for the denuded skin after burns, injuries, surgical planing, etc.—Eds.]

Formation of Vellus Hair Follicles from Human Adult Epidermis. The epidermis is the ultimate source of the cutaneous adnexa, giving rise at about the third month of fetal life to eccrine sweat glands and the primary epithelial germ from which in turn are differentiated the pilosebaceous and the apopilosebaceous unit. Classic teaching has until recently at least denied or been unaware of the potentiality of the epidermis to form adnexa in adult life, particularly in respect to the creation of new hair follicle. The genesis of new hair follicles has been recently demonstrated in adult rabbits. An example of this in adult human beings is described by Albert M. Kligman and John S. Strauss (Univ. of Pennsylvania).

(1) J. Invest. Dermat. 27:19-23, July, 1956.

i.e., the emptying of the glandular reservoir as evidenced by the appearance of sweat on the skin surface. The latter process is caused by contraction of the myoepithelium in the glands. This accounts for the response that was obtained to injection of epinephrine and norepinephrine and absence of a response to acetylcholine. Pitocin, a known smooth muscle stimulant, produced unequivocal sweating in 9 of the 10 subjects tested. Anxiety and fear were as effective in emptying the ceruminous glands as the axillary apocrine glands. Heat did not produce a response in the ceruminous glands or axillary apocrine glands. Apocrine sweat is the product of the ceruminous gland and is only one component of cerumen which also contains sebum and desquamating epithelial cells.

Studies on Growth of Bacteria in Human Ear Canal. The relation between bacteria and external otitis in man is vague. Occasionally bacteria are the direct and complete cause and antibacterial therapy as indicated by culture and sensitivity tests, effects immediate recovery. Sometimes, bacteria play only a secondary role in production o protraction of external otitis although pathogenic organisms are cultured antibacterial therapy produces only partial response. Usually though micro-organisms can be cultured from the external auditory canal they are unrelated to the disease their mere presence on culture is not diagnosti of bacterial external otitis. Knowledge of the normal bacterial flora of the ear canal is essential to evaluate any etiologic significance of organisms cultured from the diseased canal

Eldon T Perry and Anna C Nichols (Univ. of Pennsylvania) surveyed aerobic and anaerobic flora of the healthy human ear canal, studied the possible bacteriostatic property of cerumen and investigated the role of Pseudomonas aeruginosa i production of external otitis They found the resident bacterial flora in the healthy human ea canal to be remarkably constant and not to vary with geographic location, sex or season. It is composed primarily of micrococci and corynebacteria. Transient flora varies slightly with personal hygiene. Cerumen in the healthy ear canal seems not to inhibit growth of the organisms tested. Pseudomonas aeruginosa alon is unlikely to cause external otitis in pre-

( ) J Invest. Dermat. 27 165-170, September 1956.

might injure the tympanic membrane A survey was made from serial sections of biopsy specimens of the external auditory canals of over 150 subjects

The skin of the external auditory canal has three appendages ceruminous glands sebaceous glands and hairs there are no eccrine glands Histologically the ceruminous gland in man has a large lumen (compared with an eccrine sweat gland) and a wall with an inner layer of secretory cells and an outer layer of myoepithelium. Pigment granules may be identified in secretory cells of certain glands. The duct usually empties into the upper third of the hair follicle, but may open on free skin surface. There is a subepidermal layer of especially well developed sebaceous glands overlying the pad of ceruminous glands The gland can be identified in embryos infants and children but does not fully develop until puberty and may disappear in old age it shows greater development in the Negro than in the Caucasian. Hairs of the canal (tragi) vary in number but may be numerous and prominent Histologic features of the ceruminous gland resemble those of the apocrine glands of the axilla both are similar physiologically It is concluded that the ceruminous gland is an apocrine gland.

► [In addition to the stickiness of the cerumen affording protection, there is a possibility that its bitter taste also may act to discourage the lingering of insects.—Eds.]

Physiology of Apocrine (Ceruminous) Gland of Human Ear Canal was investigated by Walter B Shelley and Eldon T Perry[5] (Univ of Pennsylvania) Direct visualization of the anterior wall of the distal portion of the external auditory canal was performed on 10 normal healthy adult males who showed great response to stimulation Thorough cleansing of the canal with alcohol swabs removed all wax and detritus Gentle handling of the ear and avoidance of emotional stimuli were necessary to prevent emptying of the glands. All injections were made with 30 gauge needles Pain as a stimulus to the glands was produced by puncturing the subject s palm with a 20 gauge needle

The ceruminous gland which resembles the apocrine sweat gland has two functions One is the secretion of sweat a slow constant process of the cells the other is sweating

(5) J Invest. Dermat. 26 13-22, January 1956.

grees of inhibition of sweating were observed with graded concentrations of sodium chloride solutions. This phenomenon may have been the result of depression of the vapor pressure gradient by sodium chloride. After a period of hydration in which sweating is suppressed, the rate of insensible water loss increased markedly resulting in a rapid loss of the water of hydration from the corneum. As the rate of insensible water loss decreased during the recovery period, indicating a lower water content of the corneum, sweating reappeared.

Fatigue of Sweat Glands rather than failure of the sudomotor system accounts for the decreased rate of sweat secretion during prolonged exposur to heat according to Jørn Hes Thaysen and Irving L. Schwartz (Rockefeller Inst.)

PROCEDURE.—Four young unacclimatised healthy males were subjected to temperatures of 104-113 F and relati humidities of 60-90% Total amount of sweat secreted was estimated at 30-60 minute intervals. Local collections of sweat were obtained from entral surfaces of the forearms and the rate of flow calculated by the weight increment of filter paper disks. Prints of the sweating areas were obtained to show dispersion of glandular activity. The reactivity of sweat glands to stimulating or inhibiting substances was tested by minute injections at the site f sweat collection on the forearm, using the opposite side as a control.

The rate of sweating decreased and rectal temperature rose after 3-6½ hours of profuse sweating. The rate of decrease was mainly due to decrease in the mean flow per gland rather than t decrease in number of functioning glands. The relat e acti ties of the sweat glands remained unchanged during exposure to heat, indicating that the absolute decline in function of any single gland is proportional to it original or max mal functional capacity. Sweat output after intradermal injection of mecholyl* was diminished by preliminary prolonged reflex sweating. Local glands kept inactive by njection of mall amounts of atropine showed a definite hypersecretion compared w th those of the control side on exposure to heat. Exhau tion of the glands by i jec t n of mecholyl produced the same effect as exhaustion by heat. Further weat gland efractory to mecholyl* howed no response to heat stimulu. After a single injection f mecholyl, five to six hours were required for complete estoration of gland la function. The experiments

J Clin Invest 34 171 1725, December 955.

viously healthy ear canals. If it is an etiologic factor secondary causes such as trauma or increased environmental heat or humidity must act simultaneously

► [The evidence obtained in this study supports the concept held by most dermatologists that the normal bacterial flora of the ear canal is not ordinarily primarily responsible for otitis externa. In order for microorganisms to play a role in otitis externa, there usually must be some underlying disorder e g dermatoses such as seborrheic dermatitis and psoriasis, maceration, excoriation or other forms of trauma.

Therapy therefore to achieve best results, should be designed to cope with all known contributory factors (for example, the combination of hygroscopic, antibacterial and antiseborrheic measures with an anti-inflammatory agent such as hydrocortisone or fluorohydrocortisone) —Eds.]

Hydration of the Skin and Its Effect on Sweating and Evaporative Water Loss were studied by Clarence A Peiss, Walter C Randall and Alrick B Hertzman.[7] The uptake of water by the skin when immersed in various solutions was found to be primarily a process of hydration of the stratum corneum The amount of water uptake on the palm and sole exceeds that on other skin areas and appears to be related to the amount of cornification of the skin The rate of water evaporation from the skin surface is increased by the hydration of the stratum corneum This is true with or without sweating

Evidence was found that a barrier layer to water movement exists in the skin at the level of the stratum granulosum or stratum lucidum Below this barrier layer the cells in the spinosum contain about 70% water while cells above this barrier zone show a gradient from 40% water content in the deep corneum to 10% in the surface layers

Hydration of the stratum corneum tends to inhibit sweating on the palm and sole the amount of inhibition being related directly to the amount of hydration

The architectural arrangement of the sweat canal and its wall suggests the working hypothesis that when hydration takes place swelling of the cells lining the sweat canal results in simple mechanical obstruction of the duct This concept is supported by the following observations The hydration of highly cornified skin area was characterized by swelling obvious to the naked eye and was absent or greatly reduced on areas of low cornification When concentrated saline solutions were used as the immersion bath swelling did not appear and sweating was not inhibited Varying de

(7) J Invest Dermat 26 459-470 June 195

METHOD.—Small sheets of callus, 0.5 mm. thick, and of equal surface areas were dried to brittleness, dipped in emulsion and the excess drained off, on the assumption that the viscosities of the emulsions being equal, the same amount would adhere to each sheet. Water entered callus from the external phase of the emulsion, causing pliability in 1 hour the pliability was observed for 16 hours subsequently Various oil phases, emulsifiers and combinations of emulsifiers, and hydrophilic adjuvants were used. The preparation of 20% mineral oil and 3% cetyl alcohol emulsified with 2% sodium lauryl sulfate was used as standard of viscosity and of activity It was the least viscous substance that would give maximal results under the conditions. W ter retaining efficiency was rated from brittleness, 0 to full pliability 4+

The semipermeable film formed, i.e., the barrier to evaporation, has an efficiency varying with minimum viscosity physical characteristics of the oil phase and degree of hydrophilia of any adjuvants or secondary emulsifiers which interfere with formation of a continuous lip d film Emulsifiers affect the barrier only as they change viscosity This is not true of the oil phase or of hydrophilic adjuvants which generally decrease barrier efficiency Thus, a preparation of high viscosity may form a barrier inferior to one less viscous. This applies under conditions of low relative humidity where the callus loses water to the atmosphere Passage of water vapor into callus at high relative humidities appears uninfluenced by presence of an oil-in-water emulsion film. Certain oil-in water emulsions how th s water barrier characteristic at low humidities maintaining it for an effective period, while permitting rapid diffus on of water at high humidities. This property is not shown by water-in-oil emulsions or greases.

Examination of Epidermis by Strip Method III. Number of Keratin Cells in Human Epidermis. Rome Hunter Hermann Pinkus and Catheri e Heise Steele[2] (Detroit) p esent a method of counting the non-nucleated keratin cells of human epidermis with a fair degree of accuracy In 14 normal adults, counts ranged from 660,000 to 1,390,000/sq cm. on the forearms. Individual ariations were fourfold greater than the error of counting Counts from the two forearms differed from each other by less than 12% Counts from the shoulder or thighs were consistently about 50% less than those from the forearm in the same person. It seems that very blond persons have elat vely small numbers of cells

(2) J Invest. Dermat. 27 31-34, July 1956.

with cholinergic stimulation suggest that the degree of fatigue of the glands increases the more the demand on the secretory mechanism exceeds the simultaneous restorative capacity Fatigue of the sweat glands and defective restoration of secretory activity may well be the primary factors involved in the induction perpetuation and progression of heat stroke.

Microanatomy of Miliaria Crystallina, primary and secondary was studied by George W Hambrick Jr and Harvey Blank[9] in two patients using whole mount technic and routine tissue histologic technic. Recent studies with fresh, unfixed skin have shown clearly that the terminal part of the eccrine sweat duct has its own intrinsic walls of keratinized cells. The luminal lining consists of periodic acid Schiff positive material throughout the course of the duct. Recently this or a similar material has been suggested as a factor in the production of sweat retention in various dermatoses The authors therefore also included this material in their studies.

Hyperkeratosis of the sweat duct orifice involved in the vesicle formation was not seen. The presence of a part of the terminal sweat duct in the vesicle roof was consistently observed with its lining of periodic acid Schiff positive material Dilatation of the proximal part of the duct as it empties through the floor of the vesicle was encountered regularly No changes were observed either in human miliaria crystallina or in experimentally obstructed footpad ducts of cats that suggested periodic acid Schiff positive material to be the cause of duct obstruction

Simple rupture of a sweat duct wall without preceding obstruction distally to the site of rupture is suggested as the initial change in miliaria crystallina.

► [The findings of Hambrick and Blank do not disprove the validity of the observations of many others that miliaria crystallina results from plugging of the sweat pores and subsequent escape of sweat from the distal portion of the duct to form an intra or subcorneal vesicle.—Eds.]

Influence of Oil in Water Emulsions on Hydration of Keratin is indicated by the degree of pliability of the keratin according to J B Shelmire, Jr[1] (Southwestern Med School) Oil in water emulsions provide excellent water retaining films at low humidities and are not occlusive or macerating at higher humidities.

(9) J Invest. Dermat. 26:327 336, April, 1956.
(1) Ibid., pp. 105-109 January 1956.

bullosa, pemphigus, Senear Usher syndrome and in one with dermatitis herpetiformis a blister could be produced under suction of 400-500 mm Hg for a maximum of 30 minutes, whereas no blister could be elicited under the same conditions in control patients

Determinations of cohesion of skin layers also were carried out in various skin areas repeated in the same area for some time, in symmetrical regions and before and after topical applications of ointment, but no definite conclusions were reached. It is concluded that this method permits elimination of individual differences that constitute the disadvantage of previous technics for producing Nikolsky's sign.

[It would be interesting to use this method in various vesicular and bullous dermatoses to test the effects on the cohesion between epidermis and cutis of various agents which produce swelling of collagen, such as potassium iodide and potassium bromide topically applied or systemically administered. Such tests might produce more repeatable and accurate results than patch tests with these chemical agents —Eds]

Mechanism of Cornification in Parakeratosis, Particularly in Psoriasis, was investigated by J H Ligterink (Univ of Amsterdam) Keratin is the horny material extractable from epidermis, nails, birds quills and other cornified matter by dissolving them in alkaline solutions Many characteristics of keratin have been debated but it is currently believed that formation of keratin is an oxidative process stimulated by copper and inhibited by vitamin A The oxidative process seems to be preceded by a reduction in which SH groups occur and in which vitamin A is probably involved. Experiments were performed with eight samples of psoriatic scales, 30 fresh eye lenses of cow, a sample of hyperkeratotic human skin and commercial keratin. Each sample was tested by paper chromatography after hydrolysis, paper electrophoresis, estimation of the pH near which coagulation started and estimation of the tryptophan-tyrosine ratio The eye lens was used because most of its metabolism is based on anaerobic processes exerted by redox systems.

Proteins of psoriatic scales differ widely from those of keratins but are strikingly and constantly similar to those of a crystalline fraction of cow lenses. The final product of cornification in psoriasis probably contains little or no keratin In psoriasis and parakeratosis generally cornification

4 Dermatologica 1 301 312, November 951.

and that the number of cells increases parallel with the color of the skin Sex appears to make no difference but age and build possibly play a role The counts were not only of the right magnitude but were close to expected figures. It is estimated that keratin cells make up somewhat over 10% of the total population of the human epidermis and that reported mitotic rates are sufficient to explain the normal turnover of epidermal cells

► [These findings lend additional support to the generally accepted idea that fair-skinned persons have more sensitive skin than brunets. A thinner keratin layer could be expected to result in less protection from sunlight, primary irritants, potential allergens, etc. It would be interesting also to see whether generally there is a thinner keratin layer on the extensor than on the flexor aspects of the arms, forearms, hands, thighs and lower legs. These are the areas most commonly involved in "winter itch" eczema, nummular eczema, eczema caused by soaps, etc.—Eds.]

Determination of Cohesion of Cutaneous Layers by Means of Suction In some dermatoses cohesion of skin layers is weakened particularly in the epidermis or near the epidermocutaneous junction with scaliness and sometimes traumatic subcorneal intradermal or subepidermal blisters developing Some of these dermatoses also display the Nikolsky sign A method is proposed by Tibor Bielicky[3] (Univ of Prague) for measuring the cohesion of skin layers i e. of the force that inhibits detachment of cutaneous layers of the skin or of cellular elements from one another

METHOD.—A metal or glass bell (diameter 2.5 cm., capacity 5,000 ml., rim rounded or provided with a rubber covering) is connected by a rubber tube with a pressure chamber and vacuometer as well as with a suction pump. In certain dermatoses, particularly in those showing Nikolsky's phenomenon, a blister or erosion can be produced by the suction action of the apparatus, and the lowest values of minimal suction and minimal time sufficient to produce small vesicles or an erosion can be determined. A glass bell is preferable because it permits continuous observation when a metal bell is used, test areas must be inspected every 30 seconds. Duration of the test was not more than 30 minutes altogether

This method was used in testing 14 patients with bullous dermatoses (1 each with epidermolysis bullosa pemphigus vulgaris or bullous toxic exanthema 3 with Senear Usher syndrome 6 with dermatitis herpetiformis 4 with porphyrinuria with bullae and 9 control patients (4 with eczema 2 each of psoriasis or epidermophytosis 1 with eczema with erythroderma) In patients with epidermolysis

(3) Dermatologica 112 107 119 February 1956.

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[4] Dermatologica 111:301-312, November 1955

may stop in a reductive phase which would normally be followed by an oxidation producing keratin. This persistent reductive phase might be due to a congenital metabolic deficiency resulting in H_2O_2 deficiency

Investigations on Peptidases in Normal and Diseased Skin of Psoriasis Patients are reported by J M Paschoud, W Keller and B Schmidli[5] (Univ of Bern) The activities of three different dipeptidases (leucyl alanyl and glycylglycine dipeptidase) and of one not decidedly homogeneous tripeptidase were tested

In the normal skin of psoriatic patients the activities of these ferments were normal In psoriasis lesions leucylglycine and glycylglycine dipeptidases were markedly inhibited and alanylglycine showed an initial gradually decreasing inhibition Tripeptidase activity was normal. That activity changes were caused by inhibition and not by lack of ferments could be shown by activation of glycylglycine dipeptidase by cobalt Controls of ferment activity in several subacute-chronic inflammatory dermatoses revealed that inflammation produces more or less significant activation of ferments Inhibition of ferments in psoriasis cannot therefore be due to inflammation After para and hyperkeratotic scales were curetted off from psoriatic areas, the previously observed ferment inhibition was missing which shows that psoriatic scales contain a substance which inhibits the dipeptidases examined. In homogenates of freshly excised psoriasis lesions a precipitation occurs regularly within one to two days. After the precipitate was removed by centrifugation the previously observed inhibition of dipeptidases was not present thus proving that the unknown inhibiting substance exists in the precipitate It is therefore possible to study the exact nature of this substance.

Observations on Thiol Content of Abnormal Stratum Corneum in Psoriasis and Other Conditions It has been shown that normal stratum corneum may contain some -SH groups though much less than the malpighian layers. An increased amount of free -SH can be demonstrated if keratin is first altered or denatured. Keratinization does not involve loss of -SH groups by oxidation to -SS- but rather their apparent loss by becoming masked the -SS- of kera

(5) Arch. klin. u. exper Dermat. 203 203 216, 1956

tin, on the other hand, appears to be already present as such in the lower epidermal layers. In considering abnormal horn, psoriatic scale, for example, the question arises as to whether the relatively large content of free -SH present here could have arisen as a result of a partial failure of masking of these groups or of a partial failure of oxidation to SS-linkages.

I. A. Magnus[4] (Guy's Hosp Med. School London) demonstrated high values for freely available -SH in aqueous homogenates of the fresh scales of psoriasis, seborrheic dermatitis, chronic (psoriasiform) dermatitis of the legs and lichen simplex chronicus.

The scales of psoriasis and chronic (psoriasiform) dermatitis and normal stratum corneum were denatured by heat, drying and treatment with lauryl sulfate. Magnus found that the mean -SH value for psoriatic scale was reduced to half by boiling and that for chronic dermatitis was increased threefold. By contrast the effect of boiling on normal horn was slight, the changes being probably insignificant. It is suggested that the free -SH content in these two types of scale reflects a partial failure of masking. In the scale of chronic (psoriasiform) dermatitis the structural abnormality of keratin appears to be less than that in psoriasis. The scales from these two dermatoses showed different chemical properties.

Disruption of Tonofibrils and Intercellular Bridges by Disulfide-Splitting Agents may be related to the mechanism of blister formation according to Richard B. Stoughton and Natalie Novak (Univ of Chicago). Their work is based on previous demonstrations that disulfide groups are present in high and uniform concentration throughout the epidermis and that, on the basis of similar molecular configurations of tonofibrils and keratin, tonofibrils and intercellular bridges contain disulfide groups. The effect on the adherence of epidermal cells of heat and extremes of pH has been investigated. Sulfhydryl compounds were used to reduce disulfides.

Method.—Fresh human skin, 2×2 mm., was immersed in solutions of sulfhydryl agents or buffer at the desired pH. After incubation, fixed in 10% Formalin and processed routinely in paraffin.

( ) Brit. J. Dermat. 68 241 311, July-Aug. 1956.
( ) J. Invest. Dermat. 26 127 36, February 1956.

For thermal experiments, fresh and frozen skin sections were exposed to 59-90 C. for 60-120 seconds on an aluminum plate. Afterward, specimens were incubated at various temperatures and times, then fixed and processed routinely. Experiments with enzymic inhibitors were also done, first using 1:1000 solutions of copper, mercury, arsenous oxide, silver and fluoride ions before incubating and processing.

Sulfhydryl compounds and extremes of pH cause in vitro disintegration of tonofibrils and intercellular bridges of fresh human epidermal cells. This results in separation of rete cells from each other—"in vitro blister formation." On this basis it is most probable that disulfide groups play an important role in the integrity of intercellular bridges and cytoplasmic tonofibrils. Mild thermal stimuli release an enzymic degradation process which results in the loss of intercellular bridges and cytoplasmic tonofibrils with separation of cells from each other. The enzymic degradation can be inhibited by sulfhydryl binding agents such as copper, mercury and silver. It is postulated that intracellular catheptsins are responsible for the enzymic cytolysis. The authors propose that the integrity of the tonofibrils and intercellular bridges depends, at least in part, on maintenance of disulfide linkages and that disruption of these structures results in separation of epidermal cells from each other.

Crystalline Basis of Melanin, Keratin and Collagen was studied by E. Meirowsky[8] (Nashville, Tenn.). The crystalline structure of these substances was established long ago by roentgen spectrographs, but crystals were not found and can only be ascertained with the aid of ultrasonics, polarization and hydrogen peroxide (3-6%).

Roentgen spectrography is based on the fact that dispersion of x rays on the surface of atoms designs a pattern on photographic films: homogeneous darkness of the latter indicates amorphous material and a ringlike pattern is due to regular distribution of atoms. *Polarization aids in determining* whether structures are doubly refractive, polarizable or show structural changes not recognizable in the usual microscope. Supersonic waves are able to break into small fragments the threadlike long chains forming molecules of natural fibers. *Hydrogen peroxide dissolves melanin to some* extent and splits horny and collagen fibers into small frag-

(8) Hautarzt 7:245-248 June, 1956

ments, thus revealing the structural details of the melanin

Melanins are neither doubly refractive nor polarizable Roentgen spectrography of natural pigments (sepia, melanin of mouse melanoma and various human tumors and melanin of chorioidea) and of photosynthetic melanins (tyrosine, tryptophan and phenylalanine) shows that all pigments give a crystal pattern. Melanin, which actually may be a melanoprotein is soluble in strong acids and alkalis it can be liquefied partly by exposure to supersonic irradiation for 3-10 minutes. The peripheral parts of liquefied zones reveal crystals of varying dimensions. Smaller structures, which in polarized light appear beautifully colored and about 0.25-0.5 μ in size are called protomeres (elementary structures)

Roentgen spectrography of keratin has regularly yielded a crystalline pattern but real crystals cannot be demonstrated. In the course of investigations on transplantability of Bowen s disease to chorioallantois, material from Darier s disease and dermatitis herpetiformis was used for controls. Surprisingly material from Darier s disease was found repeatedly to cause chorioallantoic changes, which microscopically consisted of cornified epithelial cells. In polarized light, numerous crystals were seen in and between these cornified elements. In the present study finely filed nail substance, particles from clavi and psoriatic scales were examined. Exposure of thin particles of clavus to supersonic irradiation showed horny masses transformed into double, refractive protomeres which in polarized light exhibited the aforementioned color phenomenon and measured 0.5 μ or less. Psoriatic scales treated with H_2O_2 for days or weeks showed numerous protomeres. Nail substance exposed similarly to H_2O_2 or ultrasound displayed numerous protomeres and rhombus crystals with varying degrees of double refraction.

In a second passage of filtered material from Darier s disease, in the seventh passage from dermatitis herpetiformis and in passages from lupus erythematosus and Bowen disease, collagen fibers were found destroyed and substituted by innumerable polarizable crystals. Collagen fibers from embryonic tendons treated with H_2O_2 appeared in polarized light subdivided in segments, the interspaces between the latter filled with numerous protomeres Occasionally

balloon like collagen fibers were seen distended by large numbers of protomeres All these experiments observations as well as roentgen spectrography prove the crystal structure of collagen and it appears that a crystalline degeneration of collagen may exist

Are protomeres then true crystals? All protomeres are doubly refractive, double refraction meaning that a definite molecular structure a high degree of atom orientation and an oriented agglomeration of minute crystals exist. Since, according to mineralogists structures without the appearance of crystals but with a definite molecular structure are designated as crystals protomeres have to be considered real crystals apart from the fact that they occasionally show distinct crystalline forms

Fibrous Keratin Precursor from Human Epidermis I. Extraction and Physical Properties of a Fibrous Protein Found in Human Epidermis. Daphne Anderson Roe[9] (Univ of Pennsylvania) extracted a fibrous protein from human epidermis with 75% lithium bromide. The protein was dried as a film and oriented by extending strips of the film 200% of their original length The film became birefringent and showed an alpha x ray diffraction diagram similar to epidermal keratin.

Elasticity and thermal contraction studies showed the relationship of this protein to keratin myosin epidermin and fibrinogen Significant amounts of this protein were present throughout the cellular epidermis but more was found in the upper than in the lower part Very small amounts were obtained from samples of powdered callus

It is impossible to determine the role that this fibrous protein plays in epidermal differentiation but it is probable that it is a prekeratin This probability is supported by the chemical findings and more particularly by the alpha x ray diagram The extremely low disulfide content of the fibrous epidermal protein suggests that keratins become fibrous and even resistant to solvents before they are stabilized by disulfide cross linking It is thought that the protein is a keratin precursor in a fibrous form but at a stage preceding the stabilization of the molecule

Experimental Investigations on Epidermal Proliferation. To compare histochemically normal and acanthotic epider

(9) J Invest. Dermat. 27 1-8, July 1956.

mis, the course of experimentally induced epidermal proliferation was studied by Gerd Klaus Steigleder and Klaus Schultis (Univ of Frankfort)

Method.—Acanthosis induced in 196 rats of about 130 Gm. eight and 12 guinea pigs by single and repeated topical applications of gel (manufactured by Siegfried, Säckingen, Germany) hite petrolatum, dermocetyl and soft paste of zinc oxide was compared with results of vitamin A given orally and testoviron[1] intramuscularly topically applied white petrolatum plus internally given chloroquine, and mechanical rubbing. *After completion of the experiments* and at varying time intervals, 1 sq cm. skin areas of the back of the animals were excised, fixed (Carnoy solution) and stained (hematoxylin-eosin, thionine McManus and others) For study of external effects, guinea pigs, in which acanthosis is more marked, are *preferred* as search for finer details is possible. Thickness of normal epidermis averages 15 ± 3.2 μ in rats, 24 ± 8.3 μ in guinea pigs.

Results revealed identical effects after topical applications of various test substances and fter simple rubbing The resulting *epidermal proliferation apparently s not due only* to mechanical damage because it can also be produced by internally given substances. A single topical application produced rap d epidermal proliferation which was maximal after 3 days but had not d sappeared completely after 10 days the diminution of acanthosis showing apparently a wa elik course. After repeated local application differences between treated and untreated areas as well as the acanthosis factor were maximal after 24 hours and also on the 11th day with return to normal after 30 days. These findings also prove the wa like course of ep dermal proliferation. A imals *treated for 10 days* how ed *no more definite* effects on the 11th day than other animals treated only three times i e prolonged treatment did not bring about acanthotic hanges This cannot be explained satisfactorily yet (habit formation ?) Oral feeding of chloroquin prevented epidermal proliferation possibly by ction on uperficial cutaneous essels, but the direct influence on the epidermis cannot be xcluded. Seven rats rubbed once daily with pure gauze only showed epidermal prol feration In testing externally appl ed substances more cons deration must be given to the ffects of rubbing

Influence of Mod of Preparation on Acanthogenic Effect of an Ointment was studied by R. Brun Eng Bujard and

1 Arch klin u exper Dermat. 202 547-574, 1956.

W Jadassohn[2] (Univ of Geneva) The authors previously showed that *some ointments applied to the skin of guinea pigs* produce acanthosis and mitotic flare-up

METHOD —Of an ointment base (stearyl alcohol 25 0, sodium cetyl sulfate 1 0 and distilled water 200.0) 12 different lots were prepared by varying the quality of alcohol (pure or technical) and the emulsifying apparatus (vibrator mixer rotary agitator or mechanical whisk) The test substance was applied eight times in 10 days by 30 seconds massage to the shaved flank of guinea pigs biopsy specimens were taken on the 10th day The thickness of the epidermis was measured in the section mitoses were not counted.

Some lots produced no or inappreciable, others a very slight acanthosis One group produced an acanthosis which though not important, showed a thickening of the epidermis of 50% and more (petrolatum tested under the same conditions produced thickening of 160–400%) These differences were not due to possible impurities of the alcohol since the same differences were seen in lots prepared with pure alcohol Microscopic examination gave no clues since lots of the cream which were microscopically very different caused similar degrees of acanthosis Differences in acanthogenic *action of different lots was attributed to the various mechanical* devices used Lots prepared with a vibrator or mechanical whisk had definite acanthogenic effects, lots prepared with a mixer showed marked differences and lots prepared with a rotary agitator possessed no acanthogenic capacity The way of preparing a cream can influence its acanthogenic action even creams prepared with purest products and in the same manner may produce varying degrees of acanthosis

► [The importance of properly preparing topical dermatologic medications cannot be stressed enough. There is an art (a "know how") to preparing certain lotions, ointments, creams, etc., which unfortunately at least nowadays is either not known or not practiced by many pharmacists. With the rapidly increasing number of proprietary topical medicaments which are now available and which are being prescribed by physicians with increasing frequency it apparently often does not pay the pharmacist to devote the time and effort that are required to properly fill certain topical preparations.—Eds.]

Reaction to Friction of Patients with Flexural Eczema was studied by P F D Naylor[3] (Univ of London) to discover if the most gentle scratching will produce a break in the epidermis during an exacerbation

(2) Dermatologica 113 35-39 July 1956
(3) Brit. J Dermat. 67:385-391 November 1955

Acute frictional reaction.—Eight males with chronic flexural eczema were subjected to blistering technics on normal skin of the anterior middle third of the tibia, using a polythene fraction head at a vertical load of 530 Gm and a speed of 1/3 second. The skin of patients with atopic eczema is much more resistant to blister formation than that of normal persons Friction at the surface may produce necrosis in prickle cells below the surface as shown by sudden break down of the epidermis. The stratum corneum may modify the applied friction stimulus by alterations in the coefficient of friction or by increase in thickness, thereby attenuating the frictional force on the prickle cells or masking the necrosis of the cells when it occurs. Increased resistance to friction is probably due to greater resistance of the prickle cells themselves or to a change in the stratum corneum

Chronic frictional reaction.—One patient who showed an increased tolerance to friction eceived daily rubbings five days a week for three months over the same area. Afte 14 weeks rubbing epidermal thickening of the rubbed area was seen nd confirmed microscopically Hyperkeratosis, but no thicken ng of the noncornified epidermis was produced in a normal person Lichenification s more early produced if the skin is resistant to blister formation.

Response of Skin of Mice to Methyl Ether of Vitamin A and Vitamin A Palmitate during known stages of hair follicle growth was studied by Ann H. Rademacher and William Montagna (Brown Univ)

METHOD—Mice were selected at age 1½- ½ months, when the first hai growth cycle was completed and hair on the back was in the resting or telogen phase. Controlled growth of follicles was obtained by plucking the club hai s. Three regions of the back were plucked, eight and four days before and on the day of application of compounds. The entire left side of the back was not plucked. The backs were treated with 0.5 cc. methyl ether of vitamin A and 0.5 cc. tamin A palmitate, each in 95% alcohol. When club hairs are plucked, their follicles become act ve almost t once Thus at the time of pplication of compounds, the first two regions were in different stages of anagen, the third had just been plucked and growth had not begun and the left side contained follicles in telogen.

It has been cla med that u saturated compounds of vitamin A, sebum, squalene and polymers of chloroprene and isoprene produce a reversible local depilation and epidermal

(4) J. Invest Dermat. 26 69 73 January 1956

thickening in mice rats and rabbits presumably due to the inhibiting effect of the double bond on sulfhydryl metabolism These compounds produce practically no effect in the guinea pig whose hair grows dischronously rather than in phase and in which the only hairs that fall out are club hairs In the present experiments the four fields of hair growth were out of phase with each other When the compounds were applied hairs fell out only when follicles were quiescent When the follicles were active the compounds did not affect growth rate. From this it seems unlikely that these vitamin A compounds interfere in vivo with cutaneous sulfhydryl metabolism and keratinization. Histochemically demonstrable sulfhydryl groups were normal in all experimental tissues Similarly skin with growing hair is relatively unaffected by one application of 20-methylcholanthrene but skin with resting follicles become greatly damaged The effect of compounds of vitamin A and the carcinogens seems qualitatively the same Whatever the mechanism protecting the skin when hair follicles are growing this mechanism is absent when follicles are quiescent. It is concluded that the reaction of the skin to the compounds of vitamin A when the follicles are resting is a generalized nonspecific stress response to an irritating agent

Factors Influencing Incidence of Epidermal Methylcholanthrene Tumors in Mice Treated with Cortisone.—*I External applications of methylcholanthrene combined with cortisone administration and biopsy trauma*—F Herrmann R W Sherwin S D Morrill M J Rothstein and Marion B Sulzberger[8] (New York Univ Post-Grad Med School and Skin and Cancer Unit) treated 400 mice with carcinogen 20-methylcholanthrene (MCA) and with cortisone by injection and biopsy specimens were taken in certain groups

In confirmation of previous findings occurrence of skin tumors produced in mice by painting with MCA (in carbowax[8]) was accelerated by concomitant subcutaneous injections of cortisone Skin excision from the painted area resulted in similar acceleration of tumor development excisions during the first two weeks of the experiment caused greater acceleration than those performed in the third (last) week of MCA applications Maximal acceleration resulted from combining MCA paintings with both cortisone admin

(8) J Invest. Dermat. 25 403-410, December 1955.

istration and trauma. The tumors were squamous cell carcinomas, papillomas, sebaceous adenomas or occasionally sarcomas. The destructive effect of MCA on hair follicles and sebaceous glands was definitely more pronounced in cortisone-treated mice than in control animals. Regrowth of hair was impeded in the cortisone-treated mice, but not in animals with the same applications of MCA without cortisone.

II Influence of variations in timing of cortisone administration in relation to carcinogen application.—Herrmann and co-workers[8] performed experiments to determine whether acceleration in occurrence of MCA-induced tumors in mice treated with cortisone depended on timing of cortisone in relation to carcinogen applications. Cortisone was administered concomitantly with applications of MCA, before them and in a period overlapping them. Significant acceleration in occurrence of epidermal tumors was evident in mice painted with MCA (0.6%) in benzene three times a week for three consecutive weeks and concomitantly given cortisone injections (20 mg/kg body weight) five times a week during the same period.

When cortisone was administered during the first three weeks of the experiment and MCA applied during the following three weeks, there was no different tumor response between cortisone treated and control animals. This ruled out the possibility that acceleration obtained with cortisone was caused by withdrawal of the steroid. Tumor response was significantly accelerated when the last week of cortisone administration coincided with the first week of painting with MCA. A trend toward accelerated tumor response was noted in control groups in which the cortisone-dispersing liquid was injected instead of cortisone and in which injections were not discontinued before treatment with MCA.

III Studies of hair follicular cycle ("skin cycle") in relation to incidence of tumors after cortisone administration.—On consecutive days of the treatment period, at least 10 animals/day were studied by Herrmann and his colleagues and biopsy findings compared with the follicular apparatus in control animals not treated with cortisone.

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[8] J. Invest. Dermat. 23 [illegible] December [illegible] 5 [illegible] 423-438

Hair growth was at rest in more cortisone-treated than control animals In a three weeks treatment period, the difference was greater during the last two weeks. A group of mice received a single painting with MCA on the fifth day after hair plucking and continued subcutaneous cortisone injections from the day of painting In these the hair follicular activity returned to normal more promptly than in the control group

In another control group treated with neither MCA nor cortisone the follicular response to plucking was nearly the same as that during cortisone administration after painting with MCA In a parallel group in which cortisone injections were started on the fifth day after plucking the hair follicular cycle did not differ materially from that observed without cortisone. When cortisone was initiated on the day of plucking the follicular resting stage was encountered relatively early but retarded follicular growth was seen later when the cycle returned to rest in the plucked animals not treated with cortisone or given injections from the fifth day after plucking

In each of 10 mice the hair cycle was investigated on five different days beginning from the fourth week after plucking i.e. with cycle in the resting stage In five treated with cortisone during the fourth and fifth weeks follicles were at rest during the sixth week while follicular proliferation prevailed in the five controls Another 10 mice were plucked three weeks later than the preceding group and 5 received cortisone from the day of plucking when new hair growth would take place. In none was there evidence of the follicular growth three days after plucking which prevailed in the controls.

Tumor response to MCA seems definitely accelerated after cortisone administration during exposure to the carcinogen It is believed that this accelerated tumor formation is largely due to interference by cortisone with follicular hair growth Follicular epithelium is more susceptible to the carcinogenic effect of chemical agents when they are applied during the resting phase of the hair cycle than during the growing phase.

Spreading of Spherical Particles in Dermal Connective Tissue. The dermal connective tissue barrier and its recon

stitution after supramaximum doses of hyaluronidase have previously been studied under various conditions by meas uring the spread of hemoglobin injected intracutaneously immediately after death of the experimental animals. Len art Juhlin (Univ of Uppsala) studied the spreading of spherical particles of mean diameter 0.1 μ and 0.75 μ injected immediately after death in the skin of rabbits Staphylococcus hyaluronidase was given the living animal six hours or one-half hour before injection of particles. Both hydrophilic and lipophilic particles were tested.

The spreading area of 0.1 μ particles was greatly increased by hyaluronidase. In areas pretreated with the enzyme six hours earlier a hyaluronidase-insensitive barrier developed. Hydrophilic particles of mean diameter 0.75 μ showed wider spreading in hyaluronidase treated areas, whereas lipophilic particles of the same size, but with a tendency to aggregation had a considerably smaller spreading area in the enzyme-treated skin than in control areas. The functional *size of pores limiting lateral spread through* hyaluronidase-treated skin was between 0.1 and 0.6 μ.

The particles may be considered as models of bacteria and viruses By analogy with the findings viruses corresponding to the 0.1 μ particles should spread more readily in tissue affected by hyaluronidase, regardless of wettability Spreading of iruses would be inhibited by a hyaluronidase-insensitive barrier however Such an enzyme-insensitive barrier has previously been demonstrated for hemoglobin.

With the particles of 0.75 μ diameter representing bacteria, the spreading promotion by hyaluronidase in intact tissue was uncertain and no hyaluronidase insensitive barrier was obtained. In inflammatory states, phagocytosis, edema and streaming of edema fluid are also involved These result in uch tissue changes that the effect of hyaluro idase on preading during life cannot be assessed by these results.

Paper Electrophoresis of Serum Proteins in Selected Dermatoses. Mauri Feldaker Louis A. Brunsting and Bernard F McKenzie[6] (Mayo Clinic and Found.) used paper electrophoresis to study the serum of about 100 patients with various dermatoses and conditions of dermatologic interest.

(5) Arch dermat wochenschr 36 131 3, 1 56
(6) J. Invest. Dermat. 26 [illegible], April 1956.

In some instances several specimens of serum from the same patient were studied at periodic intervals and the results compared

Results of filter paper electrophoresis of serum protein tended to confirm the findings of others who have used the more complicated Tiselius method. Alterations were usually in the albumin and gamma globulin The alpha$_1$ alpha$_2$ and beta globulins generally do not change significantly nor do slight changes appear of diagnostic significance. The alpha$_1$ globulin was the least variable of any of the fractions of protein and as a rule were within the normal range.

Pemphigus vulgaris and foliaceus systemic lupus erythematosus dermatomyositis and the lupus erythematosus syndrome occurring after use of hydralazine (apresoline®) hydrochloride may be associated with normal or abnormal serum proteins Serum albumin may be greatly decreased and gamma globulin greatly increased, whether or not there is renal involvement as manifested by albuminuria in patients severely ill with lupus erythematosus Usually the degree of increase in gamma globulin is a guide to the activity of systemic lupus erythematosus and a great decrease in serum albumin suggests a poor prognosis

Dermatomyositis is generally associated with normal total protein and with normal albumin and globulin fractions slightly decreased albumin and slightly increased gamma globulin are rarely found during acute exacerbation of the disease. An abnormal pattern of protein should heighten the possibility of lupus erythematosus when it is difficult to differentiate dermatomyositis from systemic lupus erythematosus

Although pemphigus vulgaris and foliaceus usually are associated with a normal or moderately decreased serum protein hypoproteinemia hypoalbuminemia and hypergammaglobulinemia are common in patients with extensive cutaneous eruptions and severe debility

Of four patients who had the lupus erythematosus syndrome associated with use of apresoline® two had relatively normal serum proteins one had some decrease in albumin and one had the pattern seen commonly in true systemic lupus erythematosu

Infra-Red Spectroscopy II. Serous Fluid in Bullae in Brocq Duhring Disease and Pemphigus Vulgaris. Infra red spectroscopy which permits direct study of substances in their natural state was used by R. Wegmann and A. Thewes to analyze serous contents of bullae in pemphigus ulgaris and dermatitis herpetiformis since histochemical and elec trophoretic studies have yielded little knowledge of these diseases.

On exposure of test substances to a cone of infra red light, certain chemical groups absorb certain wavelengths (possess a fbration of a certain frequency) thus forming the spectral band characteristic of the groups. A number of such bands form the spectrum of the test substance. This method, already used to study lipids polysaccharides ster oids and proteins, permits not only recognition of their basic ibrations, but also changes (ntensity localization) of vi brations when substances themselves change.

Infra-red spectroscopy was done on two patients (1) a woman, 59 with dermatitis herpetiformis (Brocq-Duhring) whose serum tests (Takata Ara, Weltmann cadmium tur bidit formolgel) were more bnormal in bulla liquid than in serum and (2) a woman, 68, who had pemphigus vul garis with hyperglycemia (2.6 Gm./L.) due to mob lization of glycogen reserves against protein loss and cachexia.

Result re ealed proteins of abnormal structure in bulla l quid in the pemphigus case which could not be attributed to denaturation d ring the test. These denatured proteins doubtle contribute at least partly to the rapidly fatal evolution of pemphigus. In dermatitis herpetiformis func tional d sequilibrium manifested itself not in structure of the protein fraction but in the phosphoglucides which, how ever wer les d turbed than in pemphigus. No definite conclusion can be drawn from these findings which must be con idered with sult of biochemical examinations until confirmation i more cases ha been obtained.

► (A s pointed out by the authors, more patients must be studied by this method before it can be decided whether the abnormalities found in these two cases ar characteristic for pemphigus and dermatitis herpetiformis —Eds.)

Spectral Reflectance of Human Skin in the Region 0.7 2.6 μ, range of major interest for study of radiation burns,

In some instances several specimens of serum from the same patient were studied at periodic intervals and the results compared.

Results of filter paper electrophoresis of serum protein tended to confirm the findings of others who have used the more complicated Tiselius method Alterations were usually in the albumin and gamma globulin The alpha$_1$ alpha$_2$ and beta globulins generally do not change significantly nor do slight changes appear of diagnostic significance. The alpha$_1$ globulin was the least variable of any of the fractions of protein and as a rule were within the normal range.

Pemphigus vulgaris and foliaceus systemic lupus erythematosus dermatomyositis and the lupus erythematosus syndrome occurring after use of hydralazine (apresoline®) hydrochloride may be associated with normal or abnormal serum proteins Serum albumin may be greatly decreased and gamma globulin greatly increased, whether or not there is renal involvement as manifested by albuminuria in patients severely ill with lupus erythematosus Usually the degree of increase in gamma globulin is a guide to the activity of systemic lupus erythematosus and a great decrease in serum albumin suggests a poor prognosis

Dermatomyositis is generally associated with normal total protein and with normal albumin and globulin fractions slightly decreased albumin and slightly increased gamma globulin are rarely found during acute exacerbation of the disease. An abnormal pattern of protein should heighten the possibility of lupus erythematosus when it is difficult to differentiate dermatomyositis from systemic lupus erythematosus

Although pemphigus vulgaris and foliaceus usually are associated with a normal or moderately decreased serum protein hypoproteinemia hypoalbuminemia and hypergammaglobulinemia are common in patients with extensive cutaneous eruptions and severe debility

Of four patients who had the lupus erythematosus syndrome associated with use of apresoline® two had relatively normal serum proteins one had some decrease in albumin and one had the pattern seen commonly in true systemic lupus erythematosus

appeared. The difference between the two represented the erythemic intensity ( ) Observation of six patients with leukoderma permitted study of the erythemic response without overlapping pigmentation.

The latency time of maximal response and duration of reaction aried considerably with dosage. Edema, vesica tion, desquamation and blistering interfered strongly with the normal course of reactions Itching sensitivity (pain by touch) and pain (even without touch) occurred with doses leading to edema, desquamation and blistering Compara tive figures were obtained with doses short of producing desquamation and blistering A tendency towards desqua mation (dry fine scales) was predominant with the short ultraviolet erythema blistering occurred with middle ul traviolet erythema. Neither was produced by the long ultraviolet

The long ultraviolet responses occur without latency reaching a maximum quickly duration is variable, with erythema of a few minutes to a day and faint pigmentation for an hour or strong, lasting for a year Short and middle ultraviolet erythemas have a definit latent period of two to three hours, reaching a maximum in half a day (short) or one to two days (middle) and may subside n a few days to a few weeks Pigmentation appears after about one day at the height of the erythemic reaction, and lasts weeks to months. Occasionally both erythema and pigmentation fol- low an irregular and fluctuating course Construction of statistical distribution curves for the t me factors of ery thema and pigmentation seem useless and misleading due to the great individual ariations

* [For investigators interested in this field of endeavor the inclusion in the original article of certain technical details and experimental data ould hav been desirable. These investigations once more show how difficult it to discuss the effects of on lamps and other ultraviolet ray-producing-lamps ithout knowing much about the details of their emission at various avelengths If one adds to these differences the ery great variations in individual reactions to the different w velengths in the ultraviolet spectrum, one should not be surprised about the unpre- dictability of clinical response to therapeutic ultraviolet radiation —Eds.]

Differences in Tissue Damaging Effects of Fractional Roentgen Irradiation with Increasing and Decreasing Sin gle Doses were tudied n animal by H J Heite and K H Vle hu (Univ of Marburg) Whether in fractional x-ray treatment of cutaneous carcinoma ncreasing, equal or de

( ) Roentgen 7 13-419 September 934

is reported by John A Jacquez, John Huss Wayne McKeehan James M Dimitroff and Hans F Kuppenheim[2] (Army Med Res Lab Ft Knox Ky)

METHOD.—A spectrophotometer improved by addition of a comparison type integrating sphere was used for measurements. Vitrolite calibrated against MgO was used as a standard and compared with the volar surface of the right forearm for reflectance tests. Values were converted to reflectances relative to the reflectance of MgO Measurements were made on the skin of 11 young white males, 1 young white female 4 Negro males and 2 male Japanese.

As shown by curves reflectance of differently pigmented skins above 1.2 μ is practically identical is primarily the reflectance of a scattering component mixed with water and is dominated by the absorption bands of water In contrast to the absence of individual differences above 1.2 μ, there are striking differences below 1.2 μ, which are correlated with differences in skin pigmentation reflectance being greater in lighter skin

► [It is hoped that studies such as these will eventually lead to the development of equipment capable of reliably reading and recording the various intensities of erythema as produced in investigations of the clinical biologic effects of various forms of radiation as well as other biologic reactions. To date no such instrument which fills the bill is available —Eds.]

Time Factors of Erythema and Pigmentation, Produced by Ultraviolet Rays of Different Wavelengths, were investigated by A Bachem[3] (Univ of Illinois) An attempt was made to keep these factors separate using wavelengths of 254 (short) 297 (medium) and 365 mμ (long) ultraviolet

METHOD.—Several ultraviolet generators were used (1) mercury arc cold quartz giving 254 mμ almost pure (2) a water-cooled mercury arc, from 280 mμ into visible light, middle ultraviolet predominating and (3) water-cooled mercury arc filtered through Corning 5874 giving long ultraviolet from 334 mμ to the visible border The work was done on 30 students aged 19-23 years, white, one female Three series of seven exposures each, from one second to five minutes, were made on the flexor surface of the forearms. There had been no recent exposure to sun or artificial lamps. Measuring devices used were a photoelectric reflection meter and an erythemameter for observing the skin through a varying number of tan-colored celluloid disks. Two methods were used for separation of erythema and pigmentation. (1) Total discoloration (erythema plus pigmentation) *was observed without pressure on the skin,* and pigmentation alone was observed by exerting enough pressure through a lucite disk that the skin was bleached and erythema dis

(2) J Appl Physiol. 8 297-299 November 1955
(3) J Invest. Dermat. 25:215-218, October 1955

As far as can be judged from erythema and epilation biologic effects are not independent of turgor and blood circulation in tissues at the time of irradiation e.g. x ray effects can be decreased by tissue anemia (mechanical compression, epinephrine cold)

EXPERIMENT 2.—T find out whether the regeneration capacity of tissues remains unchanged after irradiation of compressed tissue, contact tube was used, equipped with a wooden inner part hich could be lowered for compression of the irradiated area. In a third series of rabbits 7,500 in daily doses of 500 r was pplied to animals with and without compression.

Results revealed striking differences in healing tendencies of punched-out holes. It appeared that by compression of tissues during irradiation not only thresholds of erythema and epilation were raised, but also functional damage to connective tissue and blood vessels was considerably reduced.

It had been observed that despite irradiation of erythematous tissues the damage to the latter was less significant the more cautiously repeated irradiations were gi en An attempt was therefore made to determine whether fractional tumor irradiation preceding application of higher doses has any influence on tissue damage.

EXPERIMENT 3.—In fourth series both ears of 12 rabbits were irradiated (12 15 sessions of equal single doses 1 500 each) In addition, on one side an ultraviolet erythema (Kromayer lamp compression, 15 seconds) was produced on the day before irradiation was started and on the other side after an erythematous reaction to 2,500-3,000 had begun to appear

Results showed that the healing tendency of punched-out holes was better when ultraviolet erythema was superimposed on a beginning x-ray erythema than when it was produced before the x ray series had tarted.

Th authors assume that these experiments support the theory of Wucherpfennig that fractional irradiation with initial smaller x-ray doses f llowed by subsequently increased s ngle doses after appearance of an irradiation erythema, is a satisfactory method for treating skin cancers

Value of X-ray Treatment in Eczema was investigated by J H Twiston Da ies[1] by symmetrical paired comparison in 89 patients. Nearly all patients had approximately symmetrical eczematous lesion so a treated hand or upper ex

(1) Brit J Dermat 66 291 302, September 1954

creasing single doses are more suitable is still under discussion Some authors prefer increasing (Wucherpfennig) and others equal or decreasing single doses (Bode Chaoul Wachsmann) It is not important to apply the highest possible tumor dose without surpassing the tolerance dose of surrounding tissues or to produce the strongest possible effects with a given dose Fractional irradiation rather aims at increasing the "selectivity factor i e., keeping the inevitable damage to irradiated normal tissue as small as possible and the tumor dose sufficiently effective This goal can be achieved when the

$$\text{selectivity factor} = \frac{\text{permissible dose for normal tissue}}{\text{destructive dose for tumor tissue}}$$

is greater than 1 (permissible dose for normal tissue meaning marked erythema plus slight epitheliolysis) There are two reasons for the increase of the selectivity factor with increasing fractional irradiation (1) With increased fractional irradiation normal human skin shows an increasingly incomplete cumulative action of x rays. (2) Vital tissues (e.g bone marrow) and also malignant tumors often show complete or even more than complete cumulative effects of x rays If selectivity is greater the less normal tissues are damaged the question whether increasing or decreasing fractional doses are more suitable for x ray treatment of carcinomas could then be decided by experimentally testing which of these two types of fractional irradiation causes less tissue damage.

Experiment 1 —In groups of 6-11 rabbits, a circular area 25 mm. in diameter in each ear was irradiated with daily fractional doses (contact apparatus by C. H. F Muller Hamburg which at 50 kv 5 ma. and 4 cm. target skin distance produces 2,586 r/minute) One ear of each animal was irradiated with increasing doses (300 r 10 times, 400 r 5 times and 500 r 5 times) the other ear was irradiated with decreasing doses (500 r 6 times 400 r 3 times and 300 r 11 times) totaling 7 500 r in 20 sessions. On the day after termination of irradiation, a hole 6 mm. in diameter was punched out in the center of the symmetrical irradiated areas of each ear Healing tendency was checked every three to x days with the aid of a measuring device. In a second series of rabbits the hole was punched out 52 days after conclusion of irradiation

Results in both series showed that healing was faster in ears to which fractional radiation with increasing single doses, had been applied.

Earle W. Brauer, Robert Loevinger and Vera Holmstrom[6] (New York Univ. Post-Grad. Med. School and Skin and Cancer Unit) attempted to ascertain if any differences in clinical biologic effects, as judged by erythema, would result from topical application to human skin in vivo of radioactive P^{32} as an aqueous solution in the form of blotting paper disks and in specially constructed sealed plaques. In these experiments the penetration and localization of P^{32} were demonstrated by autoradiography of tissue sections prepared from biopsy specimens.

When P^{32} solution was applied to the surface of the skin by direct pipetting or in form of a blotting paper disk, autoradiography showed no correlation between the erythematous response which is observed and the amount of P^{32} found on the surface of the skin or within the tissues.

When P^{32} was applied to the surface of the skin simultaneously as an aqueous solution, in form of a blotting paper disk and in a sealed plaque, no regular difference in biologic effect, as judged by erythema, was observed among the three methods. These findings indicate that the biologic effectiveness of P^{32} (a pure beta emitter) seems to be essentially equal whether acting from the surface or following penetration into the tissues. These findings are at variance with previous studies on thorium X (primarily an alpha emitter) in which it was shown that penetration of thorium X into the tissue definitely enhances the erythematous response.

The author believe that alpha-emitting isotopes with their highly ionizing radiation of short trajectory produce an enhanced biologic effect following their penetration into and intimate relation with the skin and its structures. On the other hand, a beta-emitting isotope, with its radiation of long trajectory produces its biologic effect when acting from the surface of the skin; the effect is apparently not significantly enhanced by the intimate relation or penetration of the isotope into the skin and its appendages.

Studies of Thorium X Applied to Human Skin. IV. Clinical and Autoradiographic Findings Following Introduction by Iontophoresis. Raul Fleischmajer and Victor H. Witten[7]

(6) J. Invest. Dermat. 26:437-447, June, 1956.
(7) Ibid. 25:223-232, October, 1955.

tremity could be compared with its fellow which received either a dummy exposure or in a very few instances no pretense of treatment. Where both upper and lower extremities were affected x rays were given to the right upper and left lower the contralateral receiving dummy exposures of the same duration. About half the patients were seen 10 days and the rest 14 days after exposure Factors were 100 kv inherent infiltration 1 mm Al half value layer 1 5 mm. Al with output at focus skin distance 25 cm., 100 r/minute single dose 150 r

Of the 89 treated, in only 1 were changes distinct enough to show where the tube had been centered. Of 83 patients with eczema given x ray treatment in whom the results were observed only 21 showed any evidence of benefit. Of these, improvement was substantial in only 5%

► [This article by J H. T D (as he has become so well known as a witty and critical abstracter of the literature for the *British Journal of Dermatology*) suggesting that present-day x ray therapy is of little value in eczema is thought provoking for many reasons. The editors would agree that x rays are not necessarily the method of choice for managing these particular dermatoses, but we have been impressed with the fact that *in many cases of eczematous eruptions proper radiation therapy is a* worthwhile adjuvant form of treatment.

For roentgen irradiation to be beneficial one must give the suitable type radiation at the right intervals to properly selected cases. In principle, superficial dermatoses must be treated with superficial forms of radiation. The quality of x radiation used by Davies, at half value layer 1.5 mm. Al, is certainly harder than that commonly used by dermatologists in the United States. This may account for his therapeutic failures when contrasted to his successes with the old gas filled tubes. The latter if we are not mistaken, used to deliver radiation of a half value layer in the range of 0.4-0.6 mm. Al—much softer than that used for this study Ordinarily since only that radiation is effective which is absorbed by the diseased tissue, it may be assumed that most of Davies radiation went way beyond the intended target. American dermatologists in general operate their x ray therapy machines at a half value layer of 0.7 1 0 mm. Al and they give approximately 75 r at weekly intervals for several weeks rather than 150 r once. Moreover there is now increasing popularity of grenz radiation in the ultrasoft range of 0.018-0.036 mm. Al half value layer and m x radiation with a half value layer less than 0.5 mm. Al.

We agree *wholeheartedly* with the suggestion that the sooner we face the facts, take back our superficial x ray therapy out of the hands of the radiologists, and design equipment suitable for dermatological use the better" In the United States this i already largely the case, since dermatologists generally use *x ray and grenz ray equipment designed for their* particular necessities.—Eds.]

Studies of Radioactive Phosphorus (P^{32}) Applied to Human Skin I. Erythema and Autoradiographic Findings Following Applications in Various Forms Victor H Witten

simplex chronicus, prurigo nodularis forms of nevus flammeus and plaques and tumors of mycosis fungoides. If increased biologic and therapeutic effects can be achieved through the iontophoresis of thorium X, it is also necessary to consider the possibility of undesirable sequelae.

[The recent clinical studies of the junior editor Wood and Loeringer using polonium, an alpha emitter in the form of plaque suggest that an erythematous response produced on human skin can result from irradiation of the epidermis alone. If this effect is conclusively proved to take place, then one must consider the possibility that the biologic changes produced not only by polonium but also those produced totally or in part by thorium X, as well as its therapeutic effects, may result from the release of diffusible substance within the epidermis alone. This substance may in turn act within the dermis to produce erythema and other alterations. It is conceivable that similar mechanism is operating in allergic eczematous reactions. If it is found eventually that the antigen-antibody interaction in this form of allergic response actually takes place within the epidermis and not in the cutis, then the possibility of diffusible substance being released by the epidermis, which acts within the epidermis and/or cutis to bring about the well known alterations, would have to be considered.—Eds.]

Effects of Tyrosine and Phenylalanine on Synthesis of Pigment in Melanocytes of Embryonic Chick Skin Cultured in Vitro are reported by John W Saunders Jr Walter C Quevedo Louis Pierro and Floyd E. Morbeck[a] (Marquette Univ)

METHOD.—Dorsal skin isolates from 7½ day old embryos of Barred Rock fowl were explanted to sterile mediums in watch glasses, either glucose agar or yolk-albumen agar. Tyrosine and phenylalanine were added. Each medium had pH of about 7.8. Isolates were taken from the back of contralateral pairs, of which one was explanted on the test medium and the other on the control. Completed preparations were incubated at 37 38 C. for 24 hours. Comparison of pigment changes in the cells after mounting the two isolates on one slide was made by team consisting of one observer and two assistants, of whom only the second could identify the tissue.

In the first series of experiments, 189 pairs of isolates were studied on mediums containing l-tyrosine. In the second series 304 pairs were studied one member of which was on medium to which l tyrosine had been added, the other on medium to which l-phenylalanine had been added. In the third series of 165 pairs l-phenylalanine alone was added to the basal medium. In the fourth series of 266 pairs both l tyrosine and l-phenylalanine were added.

Isolates of skin cultured in mediums containing l tyrosine

(a) J Nat Cancer Inst. 1 471-484, October 1 33

(New York Univ Post Grad. Med. School and Skin and Cancer Unit) attempted to increase the penetration into the skin of thorium X and its daughter products after first trying to introduce it into a test material by the galvanic iontophoretic current. It was shown that iontophoresis definitely increases the penetration of thorium X and/or its products through absorbent papers.

METHOD.—To the upper aspect of the volar surface of both forearms of each of three volunteers *a square of blotting paper saturated with 1 cc. of 0.1% NaCl solution containing 12 μc. thorium X* was applied. Similarly a square of blotting paper with saline solution but no thorium X was applied to the lower portion of the left forearm. With use of a round electrode 1.25 in. in diameter on the blotting paper with thorium X on the upper left forearm (site A) connected to the positive pole of a galvanic circuit, the area received 20 minutes of iontophoresis at 2 ma. The same procedure was carried out on the lower area of the left forearm without thorium X (site B). The right forearm with thorium X (site C) served as a second control with application of the electrode for 20 minutes, but without turning on the galvanic current. Two hours after iontophoresis, excision biopsies were made from sites A and C. The freshly excised tissues were immediately frozen on the microtome, and autoradiograms were prepared, all tissues being handled in identical fashion.

The following clinical biologic effects were noted. After removal of the blotting paper sites A and B were erythematous, but site C was not Eight hours later there was faint redness at site A but nothing at sites B or C At 30 hours the erythema at site A was more marked reaching its peak at 48 hours with some predilection for perifollicular areas sites B and C were without reaction By the 6th day pigmentation was noted only at site A as the erythema became less [illegible] for 2½ months [illegible] month The au[illegible] [illegible] ances a greater number of nuclear tracks on the surface and within the tissue for site A than for site C (without iontophoresis)

Under the conditions of the experiment, it is evident that the clinical biologic effects of erythema and pigmentation produced by iontophoresis of thorium X solution and the autoradiographic *results of biop ies of the affected areas* are related to penetration of thorium X and its daughter atoms into the skin It is suggested that this modality might increase the therapeutic effectiveness in the treatment of such dermatologic lesions as keloids thickened lesions of lichen

nase system in normal black hair matrix melanocytes blue nevi and malignant melanomas. Markedly accelerated tyrosinase uptake is shown only in malignant melanoma cells. The incorporation of C^{14} labeled tyrosine into melanocytes appears to be a specific enzymic reaction involving the tyrosinase system for the following reasons. (1) A copper binding agent and a competitive inhibitor both prevent incorporation of labeled tyrosine. (2) Incorporation of labeled tyrosine does not occur in albino hair matrix melanocytes which lack tyrosinase. (3) Such incorporation occurs only in melanized or nonmelanized malignant melanoma since other anaplastic neoplasms do not contain tyrosinase. (4) Incorporation of labeled phenylalanine and tryptophane does not occur

Use of Radioactive Tyrosine in Studying Melanotic Tumors Preliminary Report. Important investigations by Fitzpatrick and others have shown that tyrosinase (the enzyme needed for oxidation of tyrosine the precursor of melanin) exists in an active state in irradiated (x rays, ultra violet light) skin and in malignant melanomas otherwise it is inactive and inhibited. H Jaeger P Lerch and J Delacrétaz (Univ of Lausanne) attempted to determine the pigmentary activity of melanomas by the use of radioactive tyrosine. The method is not complete yet and permits only an approximate evaluation of results obtained.

METHOD.—The product used was dl-2 C^{14} tyrosine with an activity of 4.. mc./Gm. suspended in a buffer phosphate solution of 100 μg./ml. and a pH of 6.8. Sodium diethyldithiocarbamate diluted with buffer phosphate solution of 3.4 mg./ml. was used as tyrosinase inhibitor Immediately after excision of the material to be tested, part was powderized and half of it treated with a mixture of equal parts of tyrosine solution and of buffer solution the other half was treated with tyrosine solution and tyrosinase inhibitor solution. Both preparations were dried and examined with a Geiger counter From the other part of the test material frozen sections were cut and treated the same way

Each tissue fragment was thus tested by two parallel methods, with tyrosine and buffer solution and also with tyrosine and tyrosinase inhibitor solution. Results obtained by the Geiger counter revealed the intensity of tyrosine fixation by the tissue tested, i.e., tyrosinase activity These results were presented as "activity index," i.e., the ratio of radioactivity (counts/minute) between the preparation containing and that not containing the inhibitor (average of the two technics)

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(1) Dermatologica 11 371-376, Apr June 1954.

are more intensely colored than similar isolates cultured in basal media In contrast explants to mediums containing l phenylalanine rarely show more pigment than the basal medium characteristically the latter show more pigment. Synthesis of melanin by embryonic melanocytes of the chick is augmented by tyrosine and inhibited by phenylalanine. This phenylalanine inhibitory effect on melanogenesis may be reversed by tyrosine, since explants to mediums in which tyrosine and phenylalanine are combined in suitable amounts are usually as intensely pigmented as those cultured in mediums containing tyrosine alone Phenylalanine may be taken up by the differentiating melanocyte. It may inhibit melanin synthesis by competing with intracellular tyrosine for combination with tyrosinase, thus displacing the normal enzyme substrate

Histochemical Autoradiographic Method for Demonstration of Tyrosinase in Human Melanocytes Nevi and Malignant Melanoma is presented by Thomas B Fitzpatrick and Atsushi Kukita[9] (Univ of Oregon) Tyrosinase is bound to the melanin granule in the cytoplasm of the melanocyte. Tyrosine becomes attached to the enzyme and oxidation and polymerization to melanin occur on the surface of the melanin granule By the use of C^{14} labeled tyrosine as substrate conversion of water soluble tyrosine to insoluble melanin on the surface of the melanin granule permits removal of unreacted water soluble tyrosine by washing Then *it is possible to record on photographic emulsion only* the newly formed radioactive melanin thus identifying the melanocytes which contain active tyrosinase

Melanocytes containing active tyrosinase are identified by heavy *deposits of silver grains on the photographic plate.* The same melanocytes do not catalyze the conversion of labeled tyrosine to labeled melanin in the presence of tyrosinase inhibitors sodium diethyldithiocarbamate or 4-chlororesorcinol.

The autoradiographic studies show varying tyrosinase activity in normal melanocytes pigmented nevi and malignant melanomas inhibited tyrosinase system in normal epidermal melanocytes, *junctional and dermal nevi and dermal melanocytes* (mongolian spots and nevus of Ota) active tyro-

(9) J Invest Dermat 26 173-183, March, 1956.

are very slightly dopa positive, but present in normal numbers, a d (3) relative type 2, in which the number of dopa positive melanocytes is reduced. Throughout the lesion these remaining cells are enlarged and have elongated dendritic processes. The border zone in all types of vitiligo has such hypertrophied melanocytes The pathogenesis of these three types is possibly related, the relative types being a forerunner of the absolute though not all les ons progress to the absolute stage.

The authors treated 14 patients by local application of meladinine and ultraviolet radiation. Meladinine is a mixture of 8-methoxypsoralen and 8-isoamyleneoxypsoralen 1 ml. solution containing 7.5 mg of each. The solution was diluted with acetone to 12.5% of its initial concentration to prevent blistering This strength was used for the first few paintings and if no untoward reactions occurred, it was increased to 25% of the original. If this caused no erythema or blistering the patients recei ed half-strength or undiluted solution. Affected skin areas were pa nted two or three times a week. If response was slow and there were no acute reactions the patients were sometimes given some solution and told to paint themselves daily In these instances quarter-strength solution was used in summer and full-strength in winter

After painting, affected skin was exposed to ultraviolet rays and, n the later investigations to natural sunlight. Repigmentation occurred only when meladinine painting was followed by solar irradiation artificial ultrav olet rays were unsatisfactory Only relati e it ligo became repigmented as a result of treatment du to stimulation of the remaining dopa-positi e melanocytes and not to increase in number The dopa-negative melanocytes n absolute tiligo could not be ctivated by treatment.

Prognosis is more favorable in Negroes than n white persons The f rmer usually have the relative types of lesions, but even in these epigmentation appears temporary

* [A seemingly plausible explanation for some of the differences in response of vitiligo to meladinine or 8-methoxypsoralen therapy Perhaps it ill be possible to decide through such histologic examinations which vitiligo cases arrant trial ith 8-methoxypsoralen therapy and which are unsuitable for such therapy —Eds.]

Roller Tube Tissue Culture Technic in Evaluation of Primary Irritancy Producing Capacity of Topical Medicaments

Results showed an activity index of about 1 i.e., no tyrosinase activity in pigmented cellular nevi blue nevi histiocytoma pigmented seborrheic warts and pigmented nevi (Recklinghausen) In a case of ulcerated and infected prickle cell epithelioma the index was 4 (possibly because some bacteria are capable of metabolizing tyrosine, using it as a nitrogen source) Results in eight cases of malignant melanoma showed that the more malignant and progressive the tumors the greater the increase of tyrosinase (i e., increased pigment activity)

► [Grupper *et al.* (Bull. Soc. franç. dermat. et syph. 61 37 1954) also used C^{14} labeled tyrosine in vitro to demonstrate the presence of an active tyrosinase system in certain pigmented lesions.—Ed.]

Pathologic Varieties of Vitiligo and Response to Treatment with Meladinine. Vitiligo is a disorder of melanogenesis characterized by depigmented areas of otherwise normal skin Any part of the body may be affected the area involved is usually limited but occasionally large patches cover most of the body The ultimate cause is not known, but it is thought there is inhibition of tyrosinase activity of the melanocytes These dendritic pigment cells the only epidermal cells capable of producing melanin are present but inactive in vitiliginous lesions. Recently a coumarin derivative meladinine has been reported to be effective in restoring pigmentation when given locally or orally

Theoretically treatment might produce repigmentation in one or more of the following ways. (1) Melanocytes might regain tyrosinase activity (2) Melanocytes might migrate to the affected area from surrounding normal skin and replace inefficient dopa negative melanocytes (3) Functioning melanocytes might migrate from underlying unaffected hair follicles (4) In some instances vitiligo might be incomplete and some normal melanocytes remain. Hyperfunction of these cells or increase in their number due to treatment might result in repigmentation (5) Residual normal melanocytes at the periphery of a lesion when stimulated by meladinine might progressively transform the defective melanocytes in the lesion

A Jarrett and G Szabó[2] (London) distinguish three types of vitiligo histologically (1) absolute with no dopa positive melanocytes (2) relative type 1 in which melanocytes

(2) Brit. J. Dermat. 68:313-326, October 1956.

are very slightly dopa-positive but present in normal numbers, and (3) relative type 2 in which the number of dopa positive melanocytes is reduced. Throughout the lesion, these remaining cells are enlarged and have elongated dendritic processes. The border zone in all types of vitiligo has such hypertrophied melanocytes. The pathogenesis of these three types is possibly related, the relative types being a forerunner of the absolute though not all lesions progress to the absolute stage.

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After painting, affected skin was exposed to ultraviolet rays and, in the later investigations, to natural sunlight. Repigmentation occurred only when meladinine painting was followed by solar irradiation. Artificial ultraviolet rays were unsatisfactory. Only relative vitiligo became repigmented as a result of treatment, due to stimulation of the remaining dopa-positive melanocytes and not to increase in number. The dopa-negative melanocytes in absolute vitiligo could not be activated by treatment.

Prognosis is more favorable in Negroes than in white persons. The former usually have the relative types of lesions, but even in these repigmentation appears temporary.

▶ [A seemingly plausible explanation for some of the differences in response of vitiligo to meladinine or 8-methoxypsoralen therapy. Perhaps it will be possible to decide through such histologic examinations which vitiligo cases warrant a trial with 8-methoxypsoralen therapy and which are unsuitable for such therapy.—Eds.]

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Results showed an activity index of about 1, i.e., no tyrosinase activity in pigmented cellular nevi, blue nevi, histiocytoma, pigmented seborrheic warts and pigmented nevi (Recklinghausen). In a case of ulcerated and infected prickle cell epithelioma the index was 4 (possibly because some bacteria are capable of metabolizing tyrosine, using it as a nitrogen source). Results in eight cases of malignant melanoma showed that the more malignant and progressive the tumors, the greater the increase of tyrosinase (i.e., increased pigment activity).

[Grupper *et al.* (Bull. Soc. franç. dermat. et syph. 61:37, 1954) also used C^{14}-labeled tyrosine in vitro to demonstrate the presence of an active tyrosinase system in certain pigmented lesions.—Eds.]

Pathologic Varieties of Vitiligo and Response to Treatment with Meladinine. Vitiligo is a disorder of melanogenesis characterized by depigmented areas of otherwise normal skin. Any part of the body may be affected; the area involved is usually limited, but occasionally large patches cover most of the body. The ultimate cause is not known, but it is thought there is inhibition of tyrosinase activity of the melanocytes. These dendritic pigment cells, the only epidermal cells capable of producing melanin, are present but inactive in vitiliginous lesions. Recently a coumarin derivative, meladinine, has been reported to be effective in restoring pigmentation when given locally or orally.

Theoretically, treatment might produce repigmentation in one or more of the following ways: (1) Melanocytes might regain tyrosinase activity. (2) Melanocytes might migrate to the affected area from surrounding normal skin and replace inefficient dopa-negative melanocytes. (3) Functioning melanocytes might migrate from underlying unaffected hair follicles. (4) In some instances vitiligo might be incomplete and some normal melanocytes remain. Hyperfunction of these cells or increase in their number due to treatment might result in repigmentation. (5) Residual normal melanocytes at the periphery of a lesion, when stimulated by meladinine, might progressively transform the defective melanocytes in the lesion.

A. Jarrett and G. Szabo[8] (London) distinguish three types of vitiligo histologically: (1) absolute, with no dopa-positive melanocytes; (2) relative type 1, in which melanocytes

(8) Brit. J. Dermat. 68:313-326, October, 1956.

types first migrating In the first week after planting sheets of epithelium and shoots of fibroblast-like cells were noted. These rarely intermingled but migrated from different peripheral sites. The epithelium-like sheets usually occurred at the glass-plasma or glass-fluid interface In cellophane substrate cultures fibroblast-like outgrowths were usually haphazard in areas not occupied by epithelial sheets and were most common on the undersurface of th perforated cellophane

In several groups of cultures, the cell type migrating dur ing the first 2 2½ weeks appeared to be epithelial. Some explants were almost surrounded by sheets of polygonal cells in a pa ement like mosaic. Later typical fibroblast like spindle cell migrated from the explant and grew in over the sheets of epithelium level with the deep surface of the cellophane. However more often, the first cells migrating during the first 2 2½ weeks were the fibroblast-like spindle cells. When this occurred, ep thelial m gration and prolifera tion was usually scanty

In most cultures with mixed outgrowth at outset, prolif eration and migration of the two predominant cell types contin ed at comparable rates during the first two weeks. It was then noted that in the li ing unsta ned culture a large proportion of migrating sheets of epithelium began to lose apparent cellular membrane and nuclear definition in those portions of the heet nearest the explant This process con tinued f four to seven days unt l a homogeneous refractile, acell lar appearing material occupied the explant periph erally Further migration and proliferation of the epithelial sheets peripherally was then markedly slow whereas fibroblast c prolif ration continued. This e entually resulted in apparent fibroblastic overgrowth. In a few cultures established f om adult human skin this self limiting of the epithelial population was not noted.

The epithelial population as t me progressed in vitro tended toward les hesion of ind vidual cells. Identifiable epi thelial lands completely d sappeared by the ninth month in culture. From the 9th through the 18th month, flasks con taining cells of two strains of adult skin presented indiscriminate intermingling of epithelial and fibroblast-like ele ments, except immediately after ubculture. After ubcul-

and Chemicals was used by Funan Hu Clarence S Livingood and James F Hildebrand[3] (Henry Ford Hosp)

METHOD.—Fragments of infant foreskin from which the dermis had been removed were cultured, using the roller tube technic of Carrel on a clot coating a coverslip and were placed in a culture tube, and covered with nutrient fluid. They were covered, incubated at 37 C., and slowly rotated. Drugs or chemicals to be tested were introduced into the supernatant fluid 7 14 days after explantation. Contact with drugs lasted 18 or 42 hours then cultures were fixed and stained with May-Greenwald and Giemsa stains. Degree of injury induced by the test compounds was determined by the presence of sloughing and destruction of the epithelial sheet, loss of staining properties and cellular outlines, changes in the nuclear elements, such as hyperchromasia, pyknosis, and fragmentation, and changes in the cytoplasm. In unfixed cultures examined by phase contrast microscopy injury was seen as retraction of the membrane, formation of coarse granules vacuole formation in the cytoplasm and separation of intercellular spaces. Antibiotics local anesthetics, antihistamines and chemicals in various concentrations were tested.

The site of injury varied with different compounds. Some involved the cell proper cytoplasm and nucleus others the intercellular spaces The method is objective the conditions uniform and the results reproducible but the test substances must be water soluble. The 20 compounds tested varied widely in toxicity Mercuric bichloride and potassium dichromate produced complete epidermal cell injury in concentrations of 50 μg/ml whereas growing epithelium tolerated neomycin in a concentration as high as 20 000 μg/ml for 42 hours without evidence of injury

This approach is proposed as a desirable laboratory procedure for preclinical evaluation of primary irritant effects of new topical therapeutic agents and for determination of potential toxicity of industrial chemicals

Characteristics and Potentials of Long Term Cultures of Human Skin were studied by C Andrew L Bassett Virginia J Evans and Wilton R. Earle[4] who grew cells derived from human skin in continuous propagation by mass tissue culture technics for periods up to 18 months. Initial skin response to in vitro conditions varied widely No uniform lag was evident in cellular migration and proliferation. Various adult skin samples exhibited lags from three days to two weeks before the first cells migrated from the explant.

Morphologically there was also wide variation in the cell

(3) J Invest Dermat. 26 23-39 January, 1956
(4) Plast. & Reconstruct. Surg 17 421-429 June 1956.

types first migrating In the first week after planting sheets of epithelium and shoots of fibroblast-like cells were noted. These rarely intermingled but migrated from different peripheral sites. The epithelium like sheets usually occurred at the glass-plasma or glass-fluid interface. In cellophane substrate cultures, fibroblast like outgrowths were usually haphazard in areas not occupied by epithelial sheets and were most common on the undersurface of the perforated cellophane.

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Cultures of human skin from fetuses of 2½-4 months gestation never showed the wide variation and initial lag noted in adult human skin Routinely luxuriant migration and proliferation of epithelial and fibroblastic elements were obtained within the first three days after planting Both epithelium and fibroblasts seemed to emerge from the explant at about the same time. There seemed to be little tendency of the epithelium like polygonal cells to form sheets instead, migration took place as individual cells. During the six months that these fetal skin cultures were continued there were never any discrete islands of sheet epithelium.

10 MISCELLANEOUS TOPICS

Influence of Attitudes in Rehabilitation of Industrial Cases is discussed by J K Morgan and J H Twiston Davies[5] with reference to the physician and the patient Preventing invalidism arising from skin disease complicated by legal and administrative associations must lie in careful and sympathetic clinical examination at the earliest possible time and in the workman s confidence in the sincerity of opinions and advice offered. The investigation consisted of clinical interviews patch testing and particularly of taking a detailed history including physical or emotional trauma preceding appearance of the rash and the patient s emotional attitude toward the disease

Among 29 patients there was an occupational factor in the dermatosis of 19 Follow up of 26 revealed that the 3 who did not respond were working at different and less remunerative jobs. Of the 29 patients seen in 1953 and 1954 28 were at work, and 10 of these were in the occupation believed to have been the cause of the disease.

Contrary to usual experience, there were about twice as many cases of epidermal sensitivity as of primary irritant reaction. All positive patch test results were significant in that the controls had negative reactions Of the 10 patients

(5) Brit J Dermat. 68 41 51, February 1956

continuing in their original occupations, 5 demonstrated sensitivity to one of the contacts at work. Seven patients were at their original work with the responsible contact removed (two had primary irritant reactions, five had specific sensitivity). Of five in less remunerative employment, three had shown sensitivities and contacts could not be excluded from the process; the other two had unequivocal constitutional eczema.

Of the 26 followed, only 14 were completely free from skin trouble and 11 of these had had positive reactions to patch tests (8 of them occupational). These persons had to avoid the responsible contact to remain well. Only three of the eight with occupational reactions were free from dermatitis and were doing pre-accident work in full. Of the other 12, 11 kept at work and did not permit the mild skin disabilities to rule their lives.

The authors present 10 cases to illustrate epidermal sensitivity associated with employment, epidermal sensitivity not associated with employment, no epidermal sensitivity but primary irritation from contacts in employment, and no epidermal sensitivity with no occupational cause. In each instance, the effect of attitude was assessed. Reactions of the skin to patch testing seem of no greater importance than the associated mental attitude. Negative results with a suspected material were not always sufficient to convince a patient that his suspicions were unfounded.

Sometimes patch test reactions to primary irritant substances without etiologic significance but included for completeness produced an opposite effect, causing the patient to focus attention on that substance. In some persons an attitude amounts to much the same thing as a delusional state, which cannot be easily changed by argument or demonstration. The mental attitude and make-up of a patient are important in rehabilitation. Patients who remained at their old work were those who were not morbidly interested in the skin conditions and had no ulterior motive (desire for compensation). Patients were encouraged to return to work as early as possible.

[An interesting approach to an age-old problem which often confronts the practitioner and, in particular, the dermatologist. The authors point out the importance of the patients' attitude regarding the conclusions reached about the compensability of their dermatoses.

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We would like to stress the importance of a *very careful* and detailed work-up of every such case because only in this way is it possible to arrive at a *just* conclusion concerning the relation between the occupational exposure and the presenting dermatosis. Such a work-up often is time-consuming and frequently is not feasible under the conditions of mass practice in which workmen's compensation work is carried on in many places. The patient's attitude toward his disease deserves much consideration also in nonindustrial and nonoccupational dermatologic practice.—Eds.]

Oral Cytodiagnosis a simple method developed from Papanicolaou's vaginal smear method is presented by W Scholdgen[6] (Dusseldorf)

Technic.—With a rubber bulb, oral secretion is sucked into a pipet and transferred to a slide and immediately fixed by a mixture of equal parts of ether and alcohol Staining is done after 10, or preferably 60 minutes. After fixation, the specimen is rinsed with 70% then 50% alcohol and water After it is stained with Harris hematoxylin (more than nine minutes) and rinsed with distilled water staining is done with lithium carbonate solution (3 drops of saturated aqueous solution/100 ml. water) for one minute. After it is rinsed with tap water distilled water and increasing concentrations of alcohol, the slide is placed into solution OG 6 for two minutes after it is rinsed in 2 portions of 96% alcohol, into solution EA 31 for three minutes. Final rinse is in 96% alcohol and xylol-alcohol and xylol embedding follows.

For evaluation of such oral smears, the oral cytogram was used in which are entered (1) in the first column, the percentage of cells with hazy protoplasm ill-defined borders and bloated nucleus (2) in the second column, percentage of cells with curled protoplasm and medium-sized nucleus (3) in the third, the percentage of cells with flattened-out protoplasm, well defined borders and pyknotic nuclei (4) in the fourth the number of eosinophils. A shift to the right of percentage figures indicates increased effects of estrogenic (folliculin hormone) substances higher figures in column 2 indicate effectiveness of corpus luteum hormone numerical preponderance of column 1 i.e., a shift to the left, is indicative of premenstrual effects.

Investigations of the course of hormonal effects in normally menstruating women revealed the maximal estrogen blood level to occur about the 10th to 12th day the maximal corpus luteum effects about the 20th to 22d day of the normal menstrual cycle. Accordingly at the time of maximal estrogen effects at least three oral smears on successive or alternate days were prepared because maximal cellular changes could be expected. Three smears were required to recognize hormonal effects of substances to be tested in the oral cytograms.

(6) Arch. klin. u. exper Dermat 201 554-563 1955

Oral cytodiagnosis permits diagnosis of hormonal disturbances and checking of drugs with hormonal action and their effectiveness.

[It has been known for many years that the effects of estrogenic hormones extend to mucosal areas other than genital. For example, Mortimer Wright and Collip (Canad. M. A. J. 35:503, 1936) described the action of these hormones on the nasal tissues. They showed that the nasal mucosa of the intact male and female monkey responds to the administration of estrogenic substance in the manner of, and synchronously with, the changes known to occur in the nipple, sex-skin, face and back. Highly interesting from the dermatologic viewpoint, because of the possible bearing it may have on acne and other problems, is the fact that peaks of nasal activity in both immature and adult female animals, usually occurred premenstrually at intervals of about 28 days. This cyclically occurring activity was most marked in the autumn months.

The work of Scholdgen provides a means for the practical demonstration of these hormonal effects on the oral mucous membranes. The cyclic changes in the oral mucosa uncovered by him may help explain some of the lesions of the mouth which appear in relation to menses, *e.g.* herpes simplex, chancre sores and perhaps even some cases of postmenopausal burning tongue, etc.—Eds.]

Skin Hazards of Coal Mining with Particular Reference to Dermatitis, are due more to physical working conditions than to chemical irritation or sensitization, according to Geoffrey Hodgson (Cardiff, Wales) who lists factors as trauma, coal and stone dust, sweating, wet conditions and coal tattooing. Dermatitis in 404 coal miners involved primarily the hands (22.8%), lower legs (18.8%) and feet and ankles (20.0%) and less commonly the abdomen, buttocks, groins, thighs, axillae, forhead, neck and shoulders. The sites involved suggest that the two main causes of localization are friction of dirty clothes and trauma and/or sweating.

Localized and lichenified plaques of dermatitis occur on the thighs or legs from pressure of the shovel or kneeling. Secondary chemical sensitization to trace elements in the stone dust such as nickel or cobalt may also cause dermatitis. The papular nonfollicular eruption on the helmet area, under the belt, on the abdomen under the lamp battery, on the buttocks, axillary folds or groins, and backs of shoulders suggest sweating as a causal factor. Sweating also accounts for dermatitis of the feet by extension of intertrigo between the toes or dyshidrotic eruptions and encourages growth of fungi and bacteria.

Constitutional factors of personal existance are also important. The greater emotional instability of the under

(7) Brit. J. Dermat. 67:38-433, December 1955.

ground worker in a dangerous job may make him less able to stand emotional stress and make the skin more sensitive. Hazards should be reduced by improved clothing and equipment design proper skin hygiene and regular skin inspection to detect early dermatitis and permit adequate skin convalescence.

► [There may be greater than normal emotional instability of underground workers, who hold dangerous jobs, which makes them less able to withstand emotional stress. But what justifies the conclusion that these factors may make their skin more sensitive? More sensitive to what? As pointed out by the author sufficient causes can be found in the dirty clothing sweating irritation and trauma from tools and rubbing clothes, dust and dirt, various chemicals, etc., to account for the occurrence of skin diseases in coal miners.—Eds.]

Dermatologic Problems in Practice of Radiology are discussed by Jesshill Love[8] (Louisville Ky) Irradiation should be used only when justified in treatment of benign skin disorders Its use for temporary relief should be strongly opposed in such disorders as acne which recur despite repeated small doses Actual skin tolerance to repeated small doses is not known because time-dose relations are seldom reported However more than 1,200 r in six months will probably produce sequelae of cosmetic significance The danger is increased in patients who receive treatment from several doctors.

The dermatologist is trained to recognize conditions amenable to irradiation but the literature contains little physical data. The resident in radiology is familiar with the physical aspects of irradiation but would benefit by further training in diagnosis of the common skin diseases. The radiologist should be aware of the cause primary disease and possible medical management and should seek dermatologic consultation Irradiation should be an adjunct in management of dermatologic problems and should be justified by need of therapy known response or absence of an equally effective measure Minimal dosage should be given and treatment discontinued with acceptable improvement or lack of response. Careful records should be kept and close attention given to dosimetry and beam control The skin dose with back scatter time intervals between treatments field size and dose distribution should be thoroughly understood

Irradiation is of little or no value in lupus erythematosus

(8) Am. J Roentgenol. 74 1123 1132, December 1955.

actinic keratosis, benign nevi, neurofibromas hypertrichosis nevus flammeus xanthomas and dermatoses of the scalp The plexiform hemangioma usually recedes promptly after one or two small exposures to roentgen rays or radium. Carbon dioxide snow or the desiccating needle is used to blanch the marginal or residual vessels. Removal by plastic surgery is recommended for angiomas that fail to improve after 300-400 r in four months, for those located over joints or flat skull bones and for rapidly growing lesions in loose, elastic skin folds. Only small port wine stains (0.3-0.5 cm.) are treated by electrodesiccation. All others are referred for surgery as are melanomas, pigmented nevi, soft fleshy moles, brown and hairy moles, linear nevus fibromas and lipofibromas. Boils, carbuncles, cellulitis and erysipelas are treated at frequent intervals to a total dose not exceeding 300 r (air) in one week. Primary medical surgical and antibiotic measures are used.

In treatment of dermatitis, topical and medical management is most important. Occasionally irradiation may be used to control the fixed eruption after the allergy factor has been eliminated. The total dose never exceeds 300 r (air) in one month.

► [The plea made by the author radiologist, that radiologist and dermatologist work together in treating skin lesions is a proper one. As result of the current training programs, physicians who are diplomates of the American Board of Dermatology are well acquainted with the physics of the radiation they use and are able to apply this knowledge to the proper therapy of those dermatoses which are best treated by this modality

It is our impression that radiation of higher kilovoltage is being used less and less in dermatologic practice in the treatment of superficial dermatoses the shift is to lower kv radiation, i.e. less than 50 kv and as low as 10 kv. This is specialized dermatologic therapy for which the dermatologist is well trained. So that patients with dermatologic disorders receive the best possible treatment, whether it be radiation, surgery topical therapy, etc dermatologists should be consulted. In turn, dermatologists should be willing to co-operate with specialists in the other fields of medicine —Eds]

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